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Pathology

EXPERIMENTAL PATHOLOGY

599. **Pathology of Swine Exposed to Total Body Gamma Radiation from an Atomic Bomb Source**

J. L. TULLIS, B. G. LAMSON, and S. C. MADDEN. *American Journal of Pathology* [*Amer. J. Path.*] **31**, 41–71, Jan.–Feb., 1955. 32 figs., 18 refs.

The authors describe the appearance and progression of the lesions occurring in swine after exposure to approximately 700 r gamma radiation from an atomic-bomb source, a dose which was spontaneously lethal on the 7th day to all animals not previously killed. It is suggested that the changes observed are applicable to man, because the general level of radiosensitivity, the terminal picture following lethal exposure, and the size of the experimental animal all approximate to those of man.

The earliest lesions observed were mitotic arrest and necrosis of lymphoid tissue, which occurred after 4 hours. Mitosis of haematopoietic cells was arrested after 8 hours, and by the end of the 4th day most marrow cells had disappeared. The later stages of injury were characterized by multiple haemorrhages throughout the body, both into the tissues and into the lumina of hollow viscera. Ulcers in the mucosa of the alimentary canal were also frequently observed. The death of the animals was probably caused by haemorrhage and bacterial invasion resulting from the early impairment of antibacterial defences and vascular reparative mechanisms. No sex differences were noted, except that the ovaries showed minimal injury, while the spermatogonia of the testes were almost entirely destroyed.

The type and sequence of the injuries are said to be similar to those following 600 r total-body *x*-irradiation at 2,000 kVP. *Jan G. de Winter*

600. **"Paradoxical" Antinecrotic Effect of Cortisol**

H. SELYE. *Archives of Pathology* [*Arch. Path.* (*Chicago*)] **59**, 90–93, Jan., 1955. 1 fig., 6 refs.

The influence of cortisol (hydrocortisone acetate) on the irritant effect of varying dilutions of croton oil injected subcutaneously into both intact and adrenalectomized female rats was studied at the University of Montreal. The "granuloma-pouch" technique, which has already been described by the author (*J. Amer. med. Ass.*, 1953, **152**, 1207), was used to produce topical stress. An injection of 25 ml. of air was given under the shaved dorsal skin of the animal, followed immediately by injection of 0·5 ml. of croton oil in concentrations varying from 0·5% to 4%, the aim being to produce an inflammatory reaction which progressed to terminal necrosis and then to study the effect of hydrocortisone on this necrotic reaction. An aqueous suspension of microcrystals of hydrocortisone (25 mg. per ml.) was injected directly into the cavity of the granuloma pouch several days after the croton oil had been given, this interval being necessary in view of the enhanced initial necrotic effect which results when an antiphlogistic hormone is combined with the irritant (loc. cit.).

Necrosis and evacuation of the pouch contents were observed in half of the intact animals receiving 3% croton oil and in nearly three-quarters when 4% croton oil was injected. As little as 5 mg. of hydrocortisone prevented this necrosis of the pouch wall. Into one group of adrenalectomized animals croton oil only was injected, while another group of similar animals received hydrocortisone simultaneously with the croton oil. Necrosis occurred in all the animals in the former group, but was not observed in any of those given hydrocortisone.

The author concludes that while anti-inflammatory corticoids facilitate the "immediate necrosis" which tends to occur in adjacent tissues during the first 24 hours after exposure to irritants, these same corticoids can also prevent terminal necrosis in both the intact and the adrenalectomized animal. *D. G. Adamson*

601. **Intrarenal Pressure in Experimental Tubular Necrosis**

H. E. DE WARDENER. *Lancet* [*Lancet*] **1**, 580–584, March 19, 1955. 7 figs., 9 refs.

Experiments carried out at St. Thomas's Hospital, London, have provided evidence that the sustained renal ischaemia of tubular necrosis arises from vasoconstriction (initiated by some undetermined mechanism) rather than from raised renal interstitial pressure.

Necrosis of the left kidney was produced in 8 dogs by occluding the renal artery with modified Michel clips for 3 to 4½ hours under pentobarbitone anaesthesia, the right kidney being used as a control. The intrarenal pressure of both kidneys was recorded in 6 dogs 2 days later, and in 2 dogs 4 days later, again under anaesthesia, the kidneys being exposed by flank incisions: in 4 dogs they were displaced outside the muscles, and in the other 4 they were undisturbed.

Continuous and simultaneous measurements of intrarenal pressure were made in both kidneys over 3 to 8 minutes by means of 24-gauge needles filled with heparinized saline solution and joined to manometers by polyethylene tubing with an internal diameter of 0·5 mm.

Needles were inserted obliquely into cortex or medulla —in the former case usually not more than 0·5 cm. below the surface. Pressures were measured at up to 12 different sites in both kidneys. Arterial blood pressure was simultaneously measured by means of a polyethylene catheter inserted into the arch of the aorta.

The pathological changes resulting from occlusion of the left renal artery varied from complete necrosis (in one dog) to colloid casts in the medullary lumina. The occluded kidneys were firmer and heavier than the control organs.

Intrarenal pressures showed considerable scatter, especially in the damaged kidneys. The mean pressure in the ischaemic organs was 16 mm. Hg, while in the controls it was 22 mm. Hg. In 3 dogs the perfusion pressure was reduced suddenly to 20 mm. Hg for 5 minutes by occluding the descending thoracic aorta. This manœuvre substantially reduced the intrarenal pressure in both kidneys. In another 3 dogs the necrosed kidney was decapsulated and 30 minutes later intrarenal pressures were again measured. No appreciable change in pressure was noted.

The account of the experiments is followed by a most interesting discussion in which the literature is clearly surveyed. *B. G. Maegraith*

602. **The Morphology of the Spinal Cord and Posterior Root Ganglia in Anoxia.** (О морфологическом состоянии спинного мозга и спинномозговых узлов при кислородном голодании (Экспериментально-морфологические Этюды))
V. P. Kurkovskii. *Архив Патологии* [*Arkh. Patol.*] **17**, 10–21, Jan.–March, 1955. 3 figs., 5 refs.

The author reviews references in the literature to the changes produced in the spinal cord by ischaemia and reports his own findings in cats exposed, once or repeatedly, to a low barometric pressure. Most of the histological lesions seemed to be of a reversible nature. Nerve cells showed mainly hydropic change with some homogenization, most marked in the intermediate columns of the grey matter, particularly in the lumbar region. There was also partial desquamation of the ependymal lining of the central canal as well as glial proliferation around it. Slight chromatolysis was present in some of the nerve cells of the posterior root ganglia. *L. Crome*

603. **Degeneration and Regeneration in Free Muscle Grafts.** (Патоморфология свободного мышечного трансплантата и регенерационные процессы в нем)
V. V. Badmayeva. *Архив Патологии* [*Arkh. Patol.*] **17**, 35–39, Jan.–March, 1955. 3 figs., 13 refs.

Working at the Moscow Regional Clinical Research Institute, the author has studied the histological changes in grafts of striated muscle implanted on to peritoneum. It was found that some regenerative phenomena appear in such grafts after initial degeneration, and that new fibres resembling embryonic muscle develop from fragments of regenerated protoplasm. These fibres are capable of further differentiation, evidence of which is seen between the 15th and 20th days, but later degenerate. The cycle of partial destruction, growth, and differentiation is observed for 60 to 70 days, after which the graft is gradually replaced by fibrous tissue and fat. The secondary degeneration is possibly related to lack of use and innervation in the regenerating fibres. *L. Crome*

604. **The Pathogenesis of Experimental Peptic Ulcer Induced in Dogs by Atophan.** (Динамика образования и развития экспериментальной язвы желудка у собак, вызванной атофаном)
I. V. Malkiman and E. A. Rudik. *Архив Патологии* [*Arkh. Patol.*] **17**, 39–45, Jan.–March, 1955. 2 figs., 6 refs.

The authors have previously reported that the administration of "atophan" (cinchophen) in doses of 0·1 to 0·2 g. per kg. body weight to dogs leads almost invariably to the formation of gastric or, less commonly, duodenal ulcers within 10 to 15 days. The ulcers often become chronic, resembling peptic ulcer in man both in anatomical site and in histological appearance. The pathogenesis of these ulcers is discussed in the present paper from the Institute of Physiology, Moscow. One of the first changes produced by atophan is a prolonged circulatory disturbance in certain ulcer-bearing areas of the stomach, which is probably the result of the action of the drug on the central and peripheral (intramural) elements of the nervous system. This leads to dystrophy of the tissues in the affected area and peptic digestion of the mucosa. *L. Crome*

605. **The Morbid Anatomy of Pneumonia Occurring after Section of the Vagus Nerves.** (Патологическая анатомия пневмонии, возникающей после перерезки блуждающих нервов)
B. I. Monastirskaya. *Архив Патологии* [*Arkh. Patol.*] **17**, 45–49, Jan.–March, 1955. 3 figs., 12 refs.

It has been known since the beginning of the last century that section of the vagus nerves is followed by pneumonia ("vagus pneumonia"). The pathogenesis of this condition was for long a matter of dispute, some authors attributing it to vascular paralysis and others favouring loss of bronchial sensitivity and paralysis of the bronchial musculature with resulting aspiration pneumonia. The question was finally settled by Pavlov in 1896, when he combined bilateral vagotomy with section of the oesophagus, feeding his animals directly into the stomach. Under these conditions, when aspiration of food was impossible, pneumonia did not develop.

The author of the present paper, working at the Leningrad Institute of Hygiene, has resected the vagus nerves in rabbits in order to study histologically the progressive development of "vagus pneumonia". She is able to confirm that the pathogenesis of the condition depends primarily on the aspiration of vegetable particles, together with mucus and desquamated squamous epithelial cells. This aspiration process spreads very rapidly and is followed by the development of focal pneumonia with confluent areas of oedema. Vascular disturbances are secondary. "Vagus pneumonia" may be interpreted

therefore as aspiration bronchitis with focal pneumonia associated with perifocal hyperaemia, oedema, atelectasis, and emphysema. *L. Crome*

606. **Experimental Infection with the Virus of Poliomyelitis through the Gastro-intestinal Canal.** (О заражении полиомеэлитом через пищеварительный тракт)
L. P. GORSHUNOVA. *Журнал Невропатологии и Психиатрии* [*Zh. Nevropat. Psikhiat.*] **55**, 102–104, Feb., 1955. 3 figs.

Experiments were carried out in which poliomyelitis virus was administered to mice and rats with the food and also instilled into the pharynx. The subsequent period of observation was 3 months, animals being killed at intervals for examination. In those animals developing signs of infection the incubation period varied from 10 to 68 days.

The virus could be found in the central nervous system by the 6th or 7th day after administration. Where the symptoms were marked and in animals which succumbed to the infection the concentration of the virus in the central nervous system gradually increased. In the animals which recovered from the infection the concentration of the virus remained low, though it was present in the central nervous system up to 90 days after administration. The virus was also present in the faeces and mesenteric lymph nodes, its concentration in the faeces varying, though it was found up to 58 days after administration. In a number of cases the virus was present in the blood, heart, and liver, the affected organs usually showing morphological changes.

The serum of those animals in which the infection produced no symptoms nevertheless showed strong neutralizing capacity against an original Lansing strain of the virus. *A. Orley*

CHEMICAL PATHOLOGY

607. **Blood Copper and its Relationship to the Globulins**
J. N. CUMINGS, H. J. GOODWIN, and C. J. EARL. *Journal of Clinical Pathology* [*J. clin. Path.*] **8**, 69–72, Feb., 1955. 1 fig., 14 refs.

The distribution of the serum copper content between the various globulin fractions in normal blood and blood from patients with hepatolenticular degeneration has been studied at the Institute of Neurology, Queen Square, London. The globulins were fractionated from the serum by precipitation with 15%, 19·6%, and 26·8% solutions of anhydrous sodium sulphate at 40° C., paper electrophoresis confirming that the three precipitates consisted of γ, $\gamma+\beta$, and $\gamma+\beta+\alpha$ globulins. The total serum copper content averaged 132·7 μg. per 100 ml. (range 90 to 180 μg.) in 10 normal adults, and 84 to 100% of this copper was recovered from the globulins, the average proportions bound to the three fractions being: γ, 19·4% (range 6 to 36%); β, 42·3% (23 to 66%); and α, 31·0% (range 17 to 42%).

The total serum copper and globulin-bound copper values were within these limits in 4 patients with involuntary movements not due to hepatolenticular disease, one with hepatic cirrhosis, and one with obstructive jaundice. In 5 cases of hepatolenticular degeneration, in which the serum protein concentrations and patterns were normal, the total serum copper content ranged from 50 to 66 μg. per 100 ml., and only 29 to 69% was bound to globulin, 30 to 60% being found by direct measurement to be bound to albumin. In 4 of these cases 1 to 7% of the serum copper content was bound to α globulin and 11 to 58% to β globulin, whereas in the fifth case 26% was bound to α globulin, but only 8% to β globulin. The proportion of copper bound to γ globulin in the 5 cases ranged from 11 to 29%.

The oxidase activity of the serum of 3 normal subjects averaged 148 μl. of oxygen per ml. per minute, about 80% of the activity being in the β-globulin fraction, while in 2 normal subjects there was no activity in the α globulin. Of the 5 cases of hepatolenticular degeneration, there was no oxidase activity in the serum in 4 and in the fifth it amounted to only 5·4 μl. O_2 per ml. per minute. No oxidase activity was detected in the globulin fractions.

The relation of these findings to the nature of hepatolenticular degeneration is discussed. *M. Lubran*

608. **The Estimation of Evans Blue in Plasma**
G. A. BEDWELL, J. PATTERSON, and J. SWALE. *Journal of Clinical Pathology* [*J. clin. Path.*] **8**, 61–64, Feb., 1955. 1 fig., 8 refs.

A method is described in this paper from Charing Cross Hospital Medical School, London, whereby Evans (azovan) blue can be recovered quantitatively from plasma by adsorption on to alkali-treated amorphous cellulose containing "celite" and subsequent elution with 35% aqueous acetone. The procedures are carried out at about 45° C. The method gives 97% recovery and is of particular value in the estimation of plasma volume by the dye-dilution method in cases where the plasma is opalescent or haemolysed, when direct colorimetry is impracticable. The plasma volume was determined with Evans blue in 10 healthy males aged 21 to 28, the dye being estimated both by the elution method and by the direct method. The mean values obtained were 44·9 and 47·1 ml. per kg. body weight respectively.
M. Lubran

609. **The Source and Clinical Significance of Ether-soluble Bilirubin in Blood Serum.** (О происхождении и клиническом значении эфирорастворимого билирубина сыворотки крови)
N. D. MIKHAĬLOVA. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **33**, 71–75, March, 1955.

Out of 190 cases of jaundice investigated by the author, in 40 the blood was found to contain ether-soluble bilirubin; of these, 27 were cases of carcinoma of the ampulla of Vater or of the head of the pancreas, of which the total number in the series was 28, and in the remainder the ether-soluble bilirubin was present in much smaller quantities. There has been little reference to the cause or significance of this finding in the medical literature, but in 1933 Varela-Fuentes and Vian described its occurrence

in 3 cases, one of carcinoma of the ampulla of Vater, one of sarcoma of the duodenum involving the ampulla, and one of " subhepatic tumour ", while Albers *et al.* have suggested that this phenomenon is a sign of the presence of malignant disease. The present author, however, does not regard it as diagnostic of malignant disease *per se*, but as resulting from obstruction of the pancreatic duct in addition to the common bile duct, with consequent reabsorption of pancreatic enzymes into the circulation. This occurs most frequently in carcinoma of the ampulla of Vater and of the head of the pancreas, and rarely in any other condition causing jaundice.

Quantitative estimations of the total ether-soluble bilirubin content of the serum in her cases lead her to the conclusion that the presence of less than 1 mg. of ether-soluble bilirubin per 100 ml. of serum is of no significance, of 1 to 2 mg. per 100 ml. is suspicious, and of more than 2 mg. per 100 ml. is definitely indicative of combined obstruction of the pancreatic and common bile ducts and therefore of probable carcinoma in the sites indicated. Post-mortem examination in several cases in which the serum ether-soluble bilirubin content was above 2 mg. per 100 ml. confirmed the almost complete obstruction of Wirsung's duct, while the absence of this fraction of bilirubin from the serum in a small number of cases of carcinoma of the ampulla of Vater or of the head of the pancreas was explained by the exceptional functional capacity of the accessory duct or, in one case, by destruction of all pancreatic tissue before occlusion of the ducts had occurred. *L. Firman-Edwards*

610. The Diagnostic Significance of Ether-soluble Bilirubin in Blood Serum in the Presence of Jaundice. (К вопросу о диференциально-диагностическом значении обнаружения эфирорастворимого билирубина в сыворотке крови больных желтухой)
A. G. LEPYAVKO. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **33**, 75–77, March, 1955. 3 refs.

The author of this article, working independently, has confirmed the finding of Mikhaĭlova [see Abstract 609] that ether-soluble bilirubin is consistently present in the blood serum in cases of carcinoma of the head of the pancreas or of the ampulla of Vater. He points out, however, that it is important to make sure that the ether-soluble fraction actually contains bilirubin and not merely urobilin, which gives a similar colour. The diazo reaction should be used to confirm the presence of bilirubin. If urobilin alone is present, the probability is that the jaundice is not due to the above causes, urobilinaemia being commonly found in infective hepatitis, hypertrophic cirrhosis, and particularly in haemolytic jaundice. *L. Firman-Edwards*

611. The Use of Hepatic Function Tests in the Diagnosis of Amebic Abscess of the Liver
T. H. BREM. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **229**, 135–137, Feb., 1955. 16 refs.

In this paper from the Veterans Administration Hospital, Long Beach, California, the results are reported of liver function tests in 10 cases in which the presence of amoebic liver abscess was diagnosed by surgical exploration with aspiration, by isolation of *Entamoeba histolytica* from the stool, from the response to specific treatment, or (2 cases only) at necropsy. In all cases the cephalin-cholesterol flocculation, thymol turbidity, and " bromsulphalein " retention tests were performed and the serum bilirubin, alkaline phosphatase, and albumin and globulin levels were determined.

Within this group of patients the pattern was that of a raised serum phosphatase level and retention of bromsulphalein associated with normal serum bilirubin level and normal response to flocculation tests. The pattern thus fits that produced by other space-occupying lesions within the liver.

The author suggests that application of this group of function tests may be useful in the differential diagnosis of amoebic liver abscess from certain other lesions of the liver. *B. G. Maegraith*

612. A Fat Absorption Test Using Iodized Oil, with Particular Application as a Screening Test in the Diagnosis of Fibrocystic Disease of the Pancreas
F. N. SILVERMAN and H. C. SHIRKEY. *Pediatrics* [*Pediatrics*] **15**, 143–148, Feb., 1955. 1 fig., 8 refs.

The use of iodized oil in the assessment of pancreatic function is based on the assumption that the absorption of the oil, orally administered, is dependent on the presence of bile and pancreatic lipase, and that the amount absorbed can be determined from the subsequent excretion of iodine in the urine after the breakdown of the iodinated fat. A simplified test of this type is described, the technique of which is as follows. No pancreatic enzyme should be given for 48 hours before the test, but no change in dietary regimen is necessary. A fasting sample of urine is collected, and not less than 5 ml. or more than 10 ml. (0·5 ml. per kg. body weight) of " lipiodol ", which contains 40% by weight of iodine, is given by mouth or stomach tube. A single specimen of urine is collected when voided, preferably 12 to 18 hours later, and a series of dilutions made. To 0·5 ml. of each dilution and of the undiluted urine, 5 drops of 8 N nitric acid and 3 drops of 1% starch solution are then added, a positive reaction consisting in a blue colour lasting at least 5 minutes. [The dilutions given in the paper are incorrectly calculated.]

The test was carried out at the Cincinnati Children's and General Hospitals on 49 control subjects and 13 children with fibrocystic disease of the pancreas. The result was negative at all dilutions in most of the cases of fibrocystic disease and negative in dilutions greater than 1 in 4 in all of them, whereas it was positive in most of the control subjects at dilutions greater than 1 in 4. In a few debilitated control children the reaction was negative, but became positive after their condition had been improved.

The authors regard the test as a satisfactory screening test for the exclusion of fibrocystic disease of the pancreas and other conditions associated with lipase deficiency.

[The data are presented in the paper in the form of a scatter diagram from which precise figures cannot be obtained. It is not stated whether the control children were healthy or suffering from other diseases. No men-

tion is made of the effect on the test of diarrhoea or other gastro-intestinal disturbances nor, apparently, were cases of coeliac disease or steatorrhoea studied. The authors' conclusions should be accepted with reserve.]

M. Lubran

613. **On Low Acid Phosphatase Values of Patients with Known Metastatic Cancer of the Prostate**
M. LONDON, R. MCHUGH, and P. B. HUDSON. *Cancer Research* [*Cancer Res.*] **14**, 718–724, Nov., 1954. 6 figs., 11 refs.

The authors estimate that at the Institute of Cancer Research, Columbia University, about 59% of known cases of cancer of the prostate with metastases give serum acid-phosphatase values considered positive for prostatic cancer. They suggest a partial explanation for the apparently normal levels of serum acid-phosphatase activity in the other 41% of cancer patients with prostatic metastases.

The prostatic enzyme as found in the serum under physiological conditions has been shown to be unstable, and the serum of males has been shown both to inhibit the enzyme and rapidly to inactivate it. Many substances normally present in serum can inhibit acid phosphatase, and a new, intensely active inhibitor, the nature of which is obscure, has been found to develop in the laboratory reagents used in assaying the enzyme. In several instances it has been found possible to alter the level of prostatic acid phosphatase present in the serum of patients with advanced prostatic cancer by controlling the body temperature of such patients within a few degrees centigrade. Cooling for 18 hours seems to be sufficient to obtain a threefold increase in the acid-phosphatase level of the serum in a patient with known advanced prostatic cancer; it is therefore suggested that a large increase in phosphatase activity on cooling may be indicative of advanced prostatic cancer.

The possibility of employing a procedure of this type for the differentiation of curable from incurable prostatic cancer which would have a higher degree of certainty is being investigated.

L. A. Elson

HAEMATOLOGY

614. **Rise of Sedimentation Rate at Low Laboratory Temperature. Its Value as a Liver-function Test**
K. D. GUPTA. *British Medical Journal* [*Brit. med. J.*] **1**, 703–704, March 19, 1955. 18 refs.

Although the erythrocyte sedimentation rate (E.S.R.) generally increases with the temperature at which it is estimated, it has been observed that in certain cases the rate is higher at low temperatures, and the author has previously shown that this is due to a qualitative change in the euglobulin fraction of the plasma proteins. Since the flocculation reactions used as liver function tests also depend upon this fraction, an attempt has been made at the S.M.S. Medical College and Hospital, Jaipur, India, to evaluate the increase in E.S.R. at low temperatures as an index of liver disease. In 17 cases of cirrhosis of the liver, 10 cases each of infective and amoebic hepatitis, 12 cases of chronic malaria, and 4 cases of cancer of the liver the serum protein level was estimated, a variety of liver function tests were carried out (including the thymol turbidity, Takata–Ara, Weltmann, and hippuric acid synthesis tests), and the E.S.R. was determined by Westergren's method simultaneously at 37° C. and 6·7° C. If the E.S.R. at 6·7° C. was 10% higher than at 37° C. the result of the test was regarded as positive, whereas if the rate was lower than at 37° C. or the difference less than 10% the result was regarded as negative or indeterminate. In infective hepatitis the results of the E.S.R. test were negative—a finding which could not be adequately explained; but in the other diseases a high percentage of positive results was obtained, which agreed in general with those of the other tests. A further 75 cases of liver disease were examined with similar results. It is suggested that an increase in the E.S.R. when determined at low temperatures indicates extensive chronic damage to liver parenchyma, and that estimation of the E.S.R. in the cold has the advantage of being simpler than other liver function tests and gives comparable results.

R. F. Jennison

615. **The Electron-microscopical Examination of Sections of Leukaemic Cells.** (Examen des cellules leucémiques au microscope électronique par la méthode des coupes)
M. BESSIS and J. BRETON-GORIUS. *Presse médicale* [*Presse méd.*] **63**, 189–193, Feb. 9, 1955. 10 figs., 21 refs.

A technique is described which has been devised at the National Blood Transfusion Centre, Paris, for the preparation of sections of leukaemic cells for examination under the electron microscope. After fixation with osmic acid the blood is centrifuged at low speed and the deposit is dehydrated and then embedded in butyl methacrylate. Sections are cut in a special microtome with a glass blade, their thickness being of the order of 20 mμ.

Some remarkable electron micrographs of cells of the granulocyte series from cases of myeloid leukaemia are reproduced. These show the presence of large numbers of vacuoles, granules, and other bodies whose existence has not hitherto been suspected. All these structures are recognizable in both normal and leukaemic cells, but in examining cells from 3 cases of myeloid leukaemia the authors have observed certain appearances which recall those seen in cells parasitized by a virus. It is not possible in the present state of our knowledge, however, to draw any conclusions from this resemblance, which may be purely morphological.

A. W. H. Foxell

616. **The Haemolytic Activity of Cold Antibodies**
J. V. DACIE. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **48**, 211–215, March, 1955. 3 figs., 6 refs.

In an earlier paper (*J. Path. Bact.*, 1950, **62**, 241; *Abstracts of World Medicine*, 1951, **9**, 61) it was shown that some cold antibodies have unexpected haemolytic properties. The main findings were that: (1) normal erythrocytes are haemolysed if the serum–corpuscle

suspensions are suitably acidified; (2) complement is needed for fixation of antibody in the cold as well as for lysis; (3) haemolysin titres (with normal corpuscles) are much lower than the agglutinin titres; and (4) corpuscles from cases of paroxysmal nocturnal haemoglobinuria are lysed at much higher dilutions than normal corpuscles.

In the present paper the author amplifies his earlier observations. He has found a difference between cold antibodies which cause agglutination as well as lysis and the Donath–Landsteiner (D–L) antibodies of paroxysmal cold haemoglobinuria, the former being most active at *p*H 6·5 to 7·0 and the latter at *p*H 7·5. Other differences are also noted. Complement is needed for haemolysis, but both high-titre agglutinating antibodies and D–L antibodies are better absorbed if complement is present when the corpuscles are being sensitized. It may be impossible to demonstrate haemolysis if cells are sensitized at 2° C. or 20° C. in heat-inactivated serum, even if fresh normal serum is added, when the suspension is subsequently warmed. One of the author's most striking findings is that some sera containing high concentrations of cold antibodies are deficient in complement activity; serial dilutions of the patient's serum must therefore be made in fresh and acidified normal human serum before it is concluded that haemolytic activity is absent. *A. Piney*

617. **Leuco-agglutinins. IV. Leuco-agglutinins and Blood Transfusion.** [In English]
J. DAUSSET. *Vox Sanguinis* [*Vox Sanguinis* (*Amst.*)] **4**, 190–198, Dec., 1954. 15 refs.

In 85% of the cases reported in the literature in which leuco-agglutinins have been found in the serum the patient was suffering from leucopenia, and in 90% the patient had received multiple blood transfusions. The question therefore arises whether the leuco-agglutinins were also auto-antibodies and responsible for the leucopenia or were immune iso-antibodies originating from the transfusions. Evidence presented here from the National Blood Transfusion Centre, Paris, shows that both transfusion and the condition of the patient play a role in the production of leuco-agglutinins.

Out of more than 1,000 normal and 700 pathological sera tested against 10 samples of normal leucocytes, 60 were shown to contain leuco-agglutinins. In all but one of these cases the patient had received one or more (average 22) transfusions before the test, and in at least 3 cases leuco-agglutinins had been shown to be absent before transfusion, the same leucocytes being used for the agglutination tests on both occasions. In 19 cases the serum was tested against 30 to 178 different samples of leucocytes, the proportion agglutinated ranging from 55·7 to 100% and exceeding 90% in 11 cases. However, in all the 26 cases in which the serum was tested against the patient's own leucocytes the reaction was negative, suggesting that the leuco-agglutinins are immune iso-antibodies. But if this is so, it is difficult to explain why leuco-agglutinins are found almost exclusively in patients with leucopenia.

Theoretical considerations are discussed in relation to these observations and it is suggested that auto-antibodies are in fact also involved, but that more delicate techniques are required to demonstrate them. While the A and B antigens are present in the leucocytes as in the erythrocytes, they appear to be of little significance, other leucocyte antigens probably being more important for the production of leuco-agglutinins. *I. Dunsford*

MORBID ANATOMY AND CYTOLOGY

618. **Correlation of Radiological and Pathological Changes in Some Diseases of the Lung**
J. GOUGH. *Lancet* [*Lancet*] **1**, 161–162, Jan. 22, 1955. 15 refs.

For several years the author, at the Welsh National School of Medicine, Cardiff, has compared the radiological appearances in pulmonary and other diseases with the morbid anatomical changes seen in paper-mounted sections of the whole lung or a whole lobe, a procedure claimed to afford a better appreciation of the underlying pathology of the radiological changes. Thus in mitral stenosis the lung radiograph shows faint punctate shadows, denser punctate shadows, and fine parallel lines above the costophrenic angle. Examination of whole sections confirms that the faint punctations represent haemosiderin deposition; that the dense punctations are due not to heavier haemosiderin deposits, but to ossification; and that the parallel lines represent haemosiderin deposits or oedema in the interlobular septa and not plate-like areas of atelectasis. The author also refers to the need for careful correlation of radiological and pathological findings in cases of microlithiasis alveolaris pulmonum, emphysema, uraemic medullary oedema of the lung, and tuberculosis, and pleads for the long-term preservation of lung radiographs. *C. L. Oakley*

619. **Pulmonary Tuberculosis after the Prolonged Use of Chemotherapy**
O. AUERBACH. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **71**, 165–185, Feb., 1955. 7 figs., 8 refs.

In cases of pulmonary tuberculosis the author has observed a marked difference between the lung lesions in patients who have received chemotherapy, especially prolonged chemotherapy, and those in patients who have been without the benefit of such treatment—an observation which, he admits, is not shared by the majority of other workers. In the present paper from the Veterans Administration Hospital, East Orange, New Jersey, he describes his findings, the most striking of which were: greatly decreased width of the fibrous capsules around the encapsulated necrotic foci; decreased thickness of the cavity walls and of the overlying pleura; decrease in pulmonary fibrosis and emphysema; greatly decreased incidence of pulmonary arterial aneurysms and consequent decrease in massive pulmonary haemorrhage; a difference in the mode of cavity healing; and more rapid healing of the tuberculous process. Many of these, it is pointed out, are the result of the rapid and extensive clearing of the perifocal reaction.

Before the advent of chemotherapy cavity healing generally occurred by obliteration of the space, often with inspissation of the contents; " open " healing, with or without epithelization, was extremely rare. However, the author has observed " open " healing in an increasing number of cases since chemotherapy has been available, which he attributes in great part to the re-epithelization of the bronchus at the bronchocavitary junction.

E. G. Rees

620. **Modifications of Tuberculosis Lesions in Patients Treated with Isoniazid**

F. Poppe de Figueiredo and D. de Paola. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **71**, 186–192, Feb., 1955. 10 figs., 17 refs.

In this paper from the Hospital-Sanatorio Santa Maria, Rio de Janeiro, the histological features of tuberculous lung tissue removed from patients treated with isoniazid are described. The most impressive feature was the hyperaemia around tuberculous cavities and in the surrounding alveolar septa, accompanied by haemorrhage into the alveoli. This, the authors suggest, offers an explanation of the bloody sputum so often observed in patients given isoniazid. Large numbers of pleomorphic giant cells with large lipoid inclusions were found in the alveoli and bronchioles. Other features were bronchiolar hyperplasia, epithelial proliferation, and the presence in an interstitial location of lymphocytic masses the centres of which, in some instances, were occupied by epithelioid and giant cells. *E. G. Rees*

621. **Morphological Studies of Hyaline Membranes in the Newborn Infant**

W. S. Gilmer and A. M. Hand. *Archives of Pathology* [*Arch. Path.* (*Chicago*)] **59**, 207–213, Feb., 1955. 6 figs., 31 refs.

The incidence of hyaline membrane in the lung in cases of neonatal death, as reported in the literature, ranges from 21 to 90%. Opinions also differ as to the source of the membrane, some authorities maintaining that it is derived from aspirated amniotic fluid and others that it is derived from the circulating blood.

At the City of Memphis Hospitals (University of Tennessee) the present authors have studied the lungs of 10 newborn infants dying with hyaline membranes and of 5 infants and children who had died from different causes. The various staining techniques and tests used are described whereby it was demonstrated that the hyaline membrane is not fibrinous; that deoxyribonucleic acid is not constantly present; that there is no metachromasia, so that hyaluronic acid, if present, must be depolymerized; and that glycogen is absent, whereas it is present in aspirated vernix. The periodic-acid–Schiff reaction was strongly positive, however, showing that other polysaccharides are present, and the presence of a 1:2-glycol linkage is indicated by the abolition of this reaction after acetylation.

In all the lungs examined the authors were able to demonstrate, under the highest magnification, a basement membrane separate from the capillary walls in the alveolar ducts and atria and extending continuously throughout the respiratory segment, overlying the highly vascular parenchyma. In the infants dying with hyaline membranes this basement membrane stained dark blue with Ritter and Oleson's stain and the hyaline material reddish-pink. In many cases the latter was present within or beneath the former, while the basement membrane could be seen in apposition with the endothelial basement membrane of the capillary walls, also staining blue, pink-staining material lying between the two membranes; in some instances it elevated the alveolar basement membrane, separating it from the endothelial basement membrane by as much as 10 to 500 μ or more. When it was present in greater quantity the outer element became fragmented and squamous cells were then found lying within the hyaline material, whereas they were never present when the overlying basement membrane was intact. Reference is made to the findings of Low (*Anat. Rec.*, 1952, **113**, 437), who demonstrated a similar structure in the lung of the rat by electron microscopy and has since shown it to occur in other animals, including man.

It is concluded that as the hyaline material appears to be situated under the respiratory basement membrane it must be of endogenous origin, being derived either from the blood or from a change in the basement membrane itself or in the underlying connective tissue.

F. Hillman

622. **Focal Pulmonary Hemosiderosis in Rheumatic Heart Disease**

M. J. Esposito. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **73**, 351–365, March, 1955. 14 figs., 27 refs.

It is pointed out that focal pulmonary haemosiderosis is not so rare a sequel of rheumatic heart disease as some reports appear to indicate. At the New York Hospital–Cornell Medical Center examination of lung sections obtained at necropsy in 100 selected cases of rheumatic heart disease revealed 28 cases of focal haemosiderosis. Other findings at necropsy were mitral stenosis in 24 cases and aortic narrowing in 4. The incidence of haemoptysis was high, but there were no other distinctive clinical features. *J. B. Enticknap*

623. **Bronchopulmonary Lesions and Circulatory Changes.** (Lésions bronchopulmonaires et modifications circulatoires)

J. Delarue, C. Sors, J. Mignot, and J. Paillas. *Presse médicale* [*Presse méd.*] **63**, 173–177, Feb. 9, 1955. 9 figs., bibliography.

At the Laboratory of Pathological Anatomy of the Paris Faculty of Medicine the authors have studied the anastomoses between the pulmonary and the bronchial arteries in the lung. They suggest that the *Sperrarterien* of von Hayek and the glomerulus-like formations also seen in sections are more common in abnormal lungs. From their studies, which were carried out by means of radio-opaque injections and by histological examination of serial sections, they conclude that anastomoses become more frequent around such pulmonary lesions as tuberculous cavities, areas of bronchiectasis, and sites of pulmonary cancer—indeed the vas-

cularization of the last named is shown to be almost entirely from the bronchial artery. They believe that the softening of a tuberculous caseous lesion is dependent on changes in the surrounding circulatory conditions, since they found that these conditions were different from the vascular pattern demonstrated around tuberculoma of the lung. (The paper is illustrated with excellent photomicrographs and radiographs.)

A. C. Lendrum

624. **Aschoff Bodies in Left Auricular Appendages of Patients with Mitral Stenosis. Clinicopathologic Study, including Post-operative Follow-up**

B. MANCHESTER, T. M. SCOTTI, M. L. REYNOLDS, and W. H. DAWSON. *Archives of Internal Medicine* [*Arch. intern. Med.*] **95**, 231–240, Feb., 1955. 3 figs., 31 refs.

Specimens of the left auricular appendage obtained at the time of mitral valvotomy on 35 patients were examined histologically at the Armed Forces Institute of Pathology, Washington, D.C., the object being to determine the possible relationship between the changes observed and the clinical features of rheumatic heart disease. Similar specimens removed at necropsy in 57 cases, including 12 cases of old rheumatic carditis, served as controls.

Aschoff bodies were noted in 13 of the 35 cases of mitral stenosis and in 2 of the control cases—both of the latter being cases of so-called old rheumatic carditis. Non-specific inflammatory changes were observed in many cases in both groups.

No relationship could be established between clinical or other signs of rheumatic activity and the presence or absence of Aschoff bodies in the auricular appendage.

G. Loewi

625. **Foetal Fibroelastosis**

J. F. HORLEY. *British Medical Journal* [*Brit. med. J.*] **1**, 765–768, March 26, 1955. 5 figs., 28 refs.

During the last 2 years 3 cases of congenital aortic stenosis accompanied by fibroelastosis of the endocardium were seen at hospitals in the Brighton Group. The infants, apparently normal at birth, had cyanotic attacks on the 1st or 2nd day of life and died during an attack on the 4th, 5th, and 8th days respectively. Necropsy revealed aortic stenosis or atresia, left ventricular hypoplasia, dilatation and hypertrophy of the right ventricle, and little or no increase in heart weight. The left ventricular endocardium was fibrotic, being from 2 to 5 mm. thick, and histologically was composed of normal collagen and elastic tissues; there was no evidence of inflammation.

The author considers that there are two types of fibroelastosis of infancy: (1) foetal fibroelastosis, the features of which are similar to those of the cases described; and (2) infantile fibroelastosis, in which there are no valvular lesions, but the left ventricle is grossly hypertrophied and the heart weight is 3 to 5 times the normal; death in infants with this form of fibroelastosis is uncommon before the age of 3 months. It is suggested that foetal fibroelastosis is caused by anoxia of the endocardium of the left side of the heart, due, perhaps, to temporary closure of the foramen ovale before the coronary circulation is fully established.

[That cases of fibroelastosis cannot always be so sharply grouped into foetal and infantile types was shown by Still (*Lancet*, 1954, **2**, 1261), who reported cases combining features of both types.] *M. C. Berenbaum*

626. **Effects of Atherosclerosis on the Coronary Circulation**

J. B. DUGUID and W. B. ROBERTSON. *Lancet* [*Lancet*] **1**, 525–527, March 12, 1955. 1 fig., 5 refs.

In reporting a histological study, made at the University of Durham, of the effects of atherosclerosis on the coronary circulation, the authors warn that in interpreting post-mortem records it is essential to have a clear idea of the significance of narrowing of the coronary arteries. They point out that thrombosis is the cause of many examples of atherosclerosis of the coronary arteries; this is commonly repeated and may at any time be of lethal degree. The shrinkage of the non-fatal thrombus and its organization produce an intimal layer of connective tissue, generally with fatty degeneration. The related media cannot therefore undergo the usual post-mortem contraction, and if the lumen be completely encircled by a fibrous layer, then there is an over-all failure of the artery to contract, giving at necropsy the appearance of a dilated coronary artery.

The authors assume that during life the fibrous layer has had a similar effect on the elastic recoil of the artery, and that atherosclerosis ultimately leads *in vivo* to dilatation of the coronary arteries. The narrowing that occurs in the earlier stage of the thrombosis is usually localized and may well be missed by the pathologist who fails to make an exhaustive study of all the major branches of the coronary arteries. Thus many hospital records are of doubtful value.

They suggest that a total occlusion may be rapidly followed by some restoration of a functioning channel, owing in part perhaps to shrinkage of the thrombus, but mainly to dilatation (or relaxation of vascular spasm). They remark that "it is perhaps a pity that the recognition of thrombosis as a cause of cardiac pain has led to the rejection of the use of the nitrites in such cases".

A. C. Lendrum

627. **A Study of the Ultraviolet Microscopy of Renal Vascular Diseases**

S. C. SOMMERS, R. CROZIER, and S. WARREN. *Circulation* [*Circulation* (*N.Y.*)] **11**, 38–43, Jan., 1955. 3 figs., 14 refs.

A study was carried out at Boston University School of Medicine of the ultraviolet absorption properties of renal arteries and arterioles from a number [unspecified] of cases of diabetic nephropathy, chronic pyelonephritis, glomerulonephritis, benign and malignant hypertension, amyloidosis, lupus erythematosus, and periarteritis nodosa. Either Zenker-fixed or freeze-dried kidney tissue was embedded in paraffin and unstained sections, 4 μ or less in thickness, were mounted in a dry state on special slides. A series of photomicrographs of a selected field was then taken with the Polaroid colour-translating ultraviolet microscope. The magnification was $\times$2,000, and 3 sets of wave-lengths in the range

2,800 to 2,350 Ångström units were used. After photomicrography the slides were stained with haematoxylin and eosin, or with such special stains as Masson–Goldner trichrome or Mallory's aniline blue. Ultraviolet absorption was increased up to 8 times the normal in those sections in which there was necrosis of the renal blood vessels—that is, in the cases of malignant hypertension and periarteritis nodosa—but no significant increase was observed in other conditions, despite the presence of definite morphological changes in the vessel wall. These results are in contrast to the distinctive changes found by the authors in the renal glomeruli in these diseases (*Amer. J. Path.*, 1954, **30**, 919). These results are as yet unexplained. *A. Wynn Williams*

628. **Hyaline Arteriolosclerosis in the Kidney**
J. P. SMITH. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **69**, 147–168, 1955. 24 figs., bibliography.

In a study of hyaline sclerosis of the afferent and efferent renal glomerular arterioles, with special reference to benign hypertension, the author examined serial sections of kidneys from 528 consecutive necropsies carried out at the University of Manchester. These concerned 266 normotensive subjects, 226 cases of hypertension, 20 of diabetes, and 16 of transient glycosuria.

It was found that both afferent and efferent arteriolosclerosis occurred in normotensives, the incidence and severity being greater in males and increasing with age in both sexes. Afferent arteriolosclerosis did not occur more commonly in patients with early hypertension than in normotensives of similar ages, but in the late stages of hypertension its incidence and severity were greater. Efferent arteriolosclerosis was not more frequent in hypertension, but in diabetes its incidence was increased.

Histological analysis indicated that hyaline arteriolosclerosis is a degenerative change in the basement membrane and ground substance of the arteriole.

J. B. Enticknap

629. **Morphological Nervous Changes in Survivors of Severe Jaundice of the Newborn**
L. CROME. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **18**, 17–23, Feb., 1955. 6 figs., 21 refs.

630. **Tissue Changes and Tissue Diagnosis in Cryptococcosis. A Study of 26 Cases**
R. D. BAKER and R. K. HAUGEN. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **25**, 14–24, Jan., 1955. 12 figs., 11 refs.

The tissue changes in 26 cases of cryptococcosis were studied at Duke University School of Medicine and the Veterans Administration Hospital, Durham, North Carolina. In 9 cases organisms were so abundant that the lesions consisted of masses of fungi, while in 3 cases organisms were rare. Gelatinous capsules were marked in 11 cases and inconspicuous in 8. Budding was readily demonstrable where organisms were abundant and capsules prominent. The histological changes were rather varied. Giant cells and macrophages were present in the majority of cases, and intracellular organisms were usually present. Neutrophil granulocytes were present in 16 cases (numerous in 5) and absent in 10. Abscess formation was rare. Lymphocytes were present in most cases, but plasma cells were infrequently found. "Caseous" necrosis was seen in pulmonary nodules in 4 cases and in massive adrenal lesions in a further case. When the symptoms had been present for less than 8 weeks organisms were abundant, gelatinous capsules prominent, and the cellular reaction was mild; in cases of longer duration there were fewer organisms, though giant cells, macrophages, and fibrosis were more conspicuous. Microscopic tubercles, similar to those of tuberculosis, were seen occasionally. Calcification was not observed.

The authors state that these tissue changes correspond with those described in the literature, except for the absence of calcification and of large cavities and large gelatinous masses in the lungs. It is considered that *Cryptococcus neoformans* induces no perceptible inflammation when it first invades the tissues, but with continued residence it is phagocytosed by giant cells, while macrophages and lymphocytes accumulate. In comparison with other fungi this organism acts more like a foreign body than an acute inflammatory irritant. *R. B. Lucas*

631. **Histoplasmosis. Tissue Reactions and Morphologic Variations of the Fungus**
C. H. BINFORD. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **25**, 25–36, Jan., 1955. 5 figs., 12 refs.

The morphology of *Histoplasma capsulatum* and the tissue reactions to this organism were studied at the Armed Forces Institute of Pathology, Washington, D.C., in 22 fatal cases of the disseminated form of histoplasmosis and many other cases of the non-disseminated form of the disease.

Discussing tissue reactions the author states that the fungus grows prolifically in the cytoplasm of reticuloendothelial cells, which become greatly distended, and sometimes giant cells form. Caseous necrosis occurs and palisaded spindle cells border the necrotic area. Neutrophil granulocytes, plasma cells, and lymphocytes are not present. Caseous nodules or non-caseous aggregations of cells are prominent, thus mimicking the changes observed in tuberculosis or sarcoid. A proliferative pneumonitis, rather than a granulomatous type of lesion, and solitary nodules simulating very closely solitary tuberculous lesions are seen in the lungs in some cases.

H. capsulatum shows a marked affinity for the adrenal glands, these organs being involved in all but one of the 22 cases. Enlargement of the spleen is also characteristic of histoplasmosis. It is pointed out that in 3 cases in the series the kidneys were involved and in 3 there was endocarditis, while in one further case miliary granulomata were present in the myocardium.

The morphology of the fungus is described; the author states that in the literature the intracellular form of the organism is generally described, but that extracellular forms show considerable variation in morphology and in staining properties. *R. B. Lucas*

Microbiology and Parasitology

BACTERIA

632. **Bacteriological Examination of Pus from Human Actinomycosis. An Evaluation of the Agar Shake Culture Method.** [In English]
M. EIKEN. *Acta pathologica et microbiologica Scandinavica* [*Acta path. microbiol. scand.*] **36**, 228–236, 1955. 15 refs.

The author, working at the State Serum Institute, Copenhagen, has examined pus from 12 patients with cervico-facial actinomycosis and has used this material to assess the relative value of various cultural procedures. He has found that the mixed flora of the pus from these cases grows much better on blood–agar and brain–heart–agar plates incubated anaerobically in the presence of carbon dioxide than in agar shake tubes.

The specimens of pus, drawn under sterile conditions from closed abscesses, all contained other organisms besides actinomycetes. These included *Actinobacillus actinomycetem-comitans*, the so-called " corroding bacillus " of Holm, and several other Gram-negative and Gram-positive micro-organisms. One actinomycete was found in each of the specimens examined, and all but 2 strains were classified according to their fermentation reactions. In agar shake tubes growth of actinomycetes could not be demonstrated by primary cultivation for more than 3 of the 12 specimens. The germination percentage in agar shake tubes was very low for *B. actinomycetem-comitans* and the " corroding bacillus "

The author concludes that the agar shake method is unsuitable for the examination of human actinomycotic pus. *E. G. Rees*

633. **Growth Characteristics, Virulence, and Cytochemical Properties of Tubercle Bacilli Recovered from Patients Treated with Isoniazid**
R. A. PATNODE, M. C. DAIL, and P. C. HUDGINS. *American Journal of Public Health* [*Amer. J. publ. Hlth*] **45**, 451–456, April, 1955. 14 refs.

634. **Optochin in the Identification of *Str. pneumoniae***
E. F. BOWERS and L. R. JEFFRIES. *Journal of Clinical Pathology* [*J. clin. Path.*] **8**, 58–60, Feb., 1955. 6 refs.

Although " optochin " (ethylhydrocupreine hydrochloride) is too toxic for clinical use, sensitivity to the drug can be used for the identification of pneumococci instead of the bile-solubility test. At University College Hospital, London, it was found that of 243 strains of bile-soluble streptococci all except one were markedly sensitive to a solution of optochin (1 in 4,000) in tests carried out with a ditch or disk on agar plates; the one exception was a mouse-avirulent strain which showed only slight sensitivity. Only one of 452 bile-insoluble strains was similarly sensitive, although 17 strains were slightly sensitive. It is suggested that with the disk method the presence of pneumococci is easily demonstrable in overnight cultures of sputum or pus containing also *Streptococcus viridans*.

Resistance to optochin was induced in one strain, which was then found to have lost its virulence for mice but to have retained its bile-solubility.
D. G. ff. Edward

635. **The Fate of *S. typhi* in Blood Clot in Relation to the Problem of Isolation**
K. C. WATSON. *Journal of Clinical Pathology* [*J. clin. Path.*] **8**, 52–54, Feb., 1955. 7 refs.

It has already been shown (*J. clin. Path.*, 1954, **7**, 305) that in typhoid fever a higher proportion of positive cultures is obtained with blood clot cultured in bile broth containing streptokinase (100 units per ml.) than with whole blood. In further experiments it was found that when blood clot containing *Salmonella typhosa* was cultured in bile broth without streptokinase no organisms could be isolated, whereas when media containing streptokinase was used cultures were positive. It is suggested that failure to isolate the organism was due to the bactericidal action of serum adsorbed in the clot. When blood clot containing *S. typhosa* was incubated at 37° C. for 7 to 14 days there was a fall in the number of positive cultures. *D. G. ff. Edward*

636. **Effect of Chloramphenicol on the Isolation of *S. typhi* from the Blood Stream**
K. C. WATSON. *Journal of Clinical Pathology* [*J. clin. Path.*] **8**, 55–57, Feb., 1955. 14 refs.

It is generally believed that the excellent clinical response to chloramphenicol in typhoid fever is accompanied by a rapid disappearance of the organisms from the blood. This, however, is at variance with the results of an investigation carried out at Grey's Hospital, Pietermaritzburg, in which blood clot was cultured in bile broth containing streptokinase (100 units per ml.). *Salmonella typhosa* was isolated on 16 occasions from 15 out of a series of 93 cases of typhoid fever, in 2 cases after 10 and 11 days' treatment with chloramphenicol respectively. In all cases there was an adequate serum level of the antibiotic and all strains of *S. typhosa* were sensitive to the drug. A possible explanation of these positive cultures is that the organisms were phagocytosed by leucocytes and thus protected against the action of chloramphenicol. In one experiment a broth culture of *S. typhosa* was mixed with a suspension of the buffy coat from normal blood. This mixture was divided into two parts, one being pre-incubated for 4 hours at 37° C.; microscopical examination revealed intracellular organisms in this part of the mixture. Both parts were then incubated at 37° C. and cultures made at intervals. *S. typhosa* was cultured even at 24 hours from the mixture which had been pre-incubated, whereas no

organisms could be demonstrated after 4 hours from the control mixture which had not been pre-incubated to allow of phagocytosis. *D. G. ff. Edward*

PROTOZOA

637. **A Contribution to the Histotopochemistry of *Pneumocystis carinii*.** (Ein Beitrag zur Histotopochemie der *Pneumocystis carinii*)
G. BRUNS and D. BÖTTGER. *Virchows Archiv für pathologische Anatomie und Physiologie und für klinische Medizin* [*Virchows Arch. path. Anat.*] **326**, 278–295, 1955. 6 figs., bibliography.

This paper from the Pathological Institute of the University of Jena describes the results of a detailed histochemical study of *Pneumocystis carinii* in infantile plasma-cell pneumonia. The isoelectric point of various parts of the parasite was determined by staining formalin-fixed frozen sections with various fluorochromes at different *p*H values and examining them for fluorescence, and by staining with the cationic dye neutral red and the anionic dye acid fuchsin in buffer solutions at various *p*H values. [The results are in good agreement with those obtained by the abstracter (*J. Clin. Path.*, 1955, **8**, 19) with the methylene-blue extinction method.] Metachromasia was demonstrable in frozen and in paraffin sections. The Gram-positive structures were found not to be identical with nuclear substance. The presence of lipids was demonstrable by weak staining with Sudan III and nile blue sulphate, and by the detection of fluorescence after staining with rhodamin B and benzopyrene–caffeine. The periodic-acid–Schiff reaction was only partly blocked by acetylation [whereas the abstracter found complete blocking; the difference may be accounted for by differences in the period of acetylation]. No preformed aldehydes were found and the Hale stain for acid mucopolysaccharides gave a positive result in certain minor components. [These findings again are contrary to those of the abstracter, which may be due to the use of different fixatives.] The presence of ribonucleic acid is considered probable [and has been confirmed by the abstracter, who observed that treatment with ribonuclease abolished the pyroninophilia which was demonstrable without such treatment].

[This account of the authors' histochemical investigations is of great value, but their conclusion that *Pneumocystis carinii* is a yeast and not a protozoon appears to the abstracter to be unjustified. The positive granules giving a positive periodic-acid–Schiff reaction (? heterochromatin) are also demonstrable in *Toxoplasma* but not in *Leishmania*. The photomicrographs purporting to show budding are not quite convincing, whereas those published by Vaněk and Jírovec and by Herzberg *et al.* are very suggestive of binary fission.] *H. S. Baar*

638. **A New Concentration Technic for the Demonstration of Protozoa and Helminth Eggs in Feces**
W. BLAGG, E. L. SCHLOEGEL, N. S. MANSOUR, and G. I. KHALAF. *American Journal of Tropical Medicine and Hygiene* [*Amer. J. trop. Med. Hyg.*] **4**, 23–28, Jan., 1955. 5 refs.

639. **Survival of Cysts of *Endamoeba histolytica* in Human Feces under Low-temperature Conditions**
S. L. CHANG. *American Journal of Hygiene* [*Amer. J. Hyg.*] **61**, 103–120, Jan., 1955. 3 figs., 22 refs.

A study was made at Harvard University to determine the survival of cysts of *Entamoeba histolytica* in human faeces when exposed to temperatures around freezing point. It was found that cysts survive longest (62·5 days) when stored at 0° C., but that the survival time decreases rapidly with reduction of the storage temperature. Faeces freeze at about −2° C., and maintaining this temperature for 30 minutes suffices to kill any cysts that are present; but the time taken to achieve this temperature throughout, and likewise the survival time of the cysts, increase in proportion to the increase in mass of faeces. The death of a cyst is caused by crystallization of its water content, but a slow rate of freezing does not increase survival, as occurs with plasmodia, trypanosomes, and leishmaniae. *R. Crawford*

FUNGI

640. **Use of Periodic Acid–Schiff Stain in Identification of Pathogenic Fungi in Tissues**
G. F. STARR, C. J. DAWE, and L. A. WEED. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **25**, 76–83, Jan., 1955. 4 figs., 12 refs.

An investigation was undertaken at the Mayo Clinic to determine how far the use of the periodic-acid–Schiff (P.A.S.) method of staining alone could assist in the identification of fungi in tissues.

In one series of 54 cases an attempt was made to discover fungi by the P.A.S. method in pulmonary lesions which had previously yielded no organisms on culture, animal inoculation, or histological examination with other stains; four of these were known positive controls. In a second series of 31 cases tissue sections of granulomata were examined; these had previously been found positive for fungi on culture, but not on microscopical examination. The sections were cut from the original paraffin blocks; serial sections were not examined, so that the procedure might be comparable to that adopted for routine histological diagnosis.

In only one case in the first series was an organism found (believed to be *Histoplasma capsulatum*) which had not been recognized previously by routine histological or bacteriological methods. In the second series there were 7 cases from which *H. capsulatum* had been cultured; organisms were demonstrated in 5 of these by the P.A.S. method. Out of 6 cases from which *Blastomyces dermatitidis* had been cultured, 5 showed the organisms in P.A.S. preparations. Out of 3 specimens yielding *Sporotrichum schenckii* on culture the organisms were found in only one, and out of 14 yielding *Coccidioides immitis* on culture the P.A.S. method revealed those organisms in 9. *Cryptococcus neoformans* was recognized morphologically as such in the single case from which it had been cultured. Thus out of 31 culture-positive cases the corresponding organism was demonstrated by the P.A.S. technique in 21.

The authors conclude that the P.A.S. method is of definite value within certain limits, but that it must remain a supplement to culture methods. In any case artefacts may closely simulate certain pathogenic fungi, and it is not always possible to identify species correctly by morphological methods alone. Furthermore, non-mycotic organisms are not identifiable by the P.A.S. technique. *R. B. Lucas*

SEROLOGY AND IMMUNOLOGY

641. **Influenza B in Boston, 1952. Isolations of Virus and Serologic Studies in Patients, Including a Study of Antigenic Differences among Influenza B Viruses Isolated in Boston from 1945 to 1952**
M. FINLAND and M. W. BARNES. *American Journal of Hygiene* [*Amer. J. Hyg.*] **61**, 24–39, Jan., 1955. 40 refs.

In a Boston influenza epidemic lasting from January to March, 1952, virus was isolated from throat washings in 9 of 14 acute cases admitted to the Boston City Hospital, and paired acute and convalescent sera from 30 acute cases were examined serologically. Some of the viruses, after further allantoic passages, were used for the preparation of immune rabbit sera for comparison with other Boston and "standard" strains. The results of haemagglutination-inhibition and complement-fixation tests, of neutralization tests *in ovo* with sera of patients, and of comparison of strains by neutralization of rabbit antisera are set out in detail.

A table of antigenic ratios giving the interrelationship between strains on a percentage basis indicates that strains isolated in Boston since 1943 did not show so close a relationship to each other when egg neutralization tests in rabbit antisera were used for the comparison as was inferred by previous workers in various countries from haemagglutination-inhibition tests with ferret, rabbit, or chicken antisera. While strains isolated in Boston since 1943 show certain similarities, distinct differences are observed from year to year and even in the same year, the possible inference being that there is a continuous variation in the antigenic pattern of the influenza-B virus. While cross-neutralization tests with rabbit antisera clearly differentiated the various influenza-B strains, this was not the case with adult convalescent sera. The more specific antibody response of children requires that recent strains be employed for vaccine production, in that they are more likely to be antigenically close to the strains active in an epidemic. *R. Crawford*

642. **Laboratory Tests following Vaccination against Influenza.** (Ricerche di laboratorio in seguito a vaccinazione contro l'influenza)
I. ARCHETTI. *Rendiconti Istituto superiore di sanità* [*R.C. Ist. sup. Sanità*] **17**, 991–998, 1954. 2 figs., 8 refs.

This report from the Institute of Hygiene, Rome, describes the appearance of antibodies in the serum of subjects inoculated with various monovalent influenza vaccines. Both the haemagglutination-inhibition test and the neutralization test in eggs were employed. The vaccines were prepared from two strains of virus—A:England/1/51 and FM1—each being used in two strengths and four groups of 50 individuals inoculated. Sera were tested for antibodies before inoculation and again 14 days after.

Haemagglutination-inhibition tests showed that the antibodies produced in the subjects inoculated with A:England/1/51 were also active against FM1, the titres being of the same order. But the antibodies produced by the subjects given the FM1 vaccine were not nearly so active against A:England/1/51. The rise in titre with the haemagglutination-inhibition test was slightly greater than with the neutralization test in subjects given the FM1 vaccine, but the neutralization test in eggs showed a much greater increase in titre in the groups given A:England/1/51 vaccine, the titres being measured against the homologous virus. The author points out that these differences in titre probably indicate that different antibodies are estimated by the two techniques. *R. F. Jennison*

643 **Complement-fixation Reaction in *Pneumocystis* Pneumonia.** (Komplement - bindungs - Reaktion bei Pneumozysten-Pneumonien)
K. BÁRTA, Č. DVOŘÁČEK, and A. KADLEC. *Schweizerische Zeitschrift für allgemeine Pathologie und Bakteriologie* [*Schweiz. Z. allg. Path. Bakt.*] **18**, 22–32, 1955. 25 refs.

The authors, working at Palacký University, Czechoslovakia, prepared 10 antigens from the dried lungs of children who had died of interstitial plasma-cell pneumonia due to *Pneumocystis carinii*, and 5 from cultures of moulds which grew on such lungs. With none of the antigens from mould-cultures was a positive complement-fixation reaction obtained with serum from cases of *Pneumocystis* pneumonia. The antigens from dried lung tissue on the other hand gave positive but variable results. Repeated preliminary treatment of the tissue with acetone followed by ethanol extraction appears to be essential. With a good antigen a positive reaction was obtained in 31 out of 34 cases of *Pneumocystis* pneumonia verified at necropsy, whereas among 22 control cases the reaction was positive in only 2, both of them cases of interstitial pneumonia of doubtful origin. Among 66 patients with a definite clinical diagnosis of *Pneumocystis* pneumonia a positive reaction was obtained in 55 cases, whereas out of 258 suspected cases only in 55 was the reaction positive.

The complement-fixation reaction appears to be of value in the differentiation of primary atypical pneumonia from *Pneumocystis* pneumonia. The results of investigations carried out on serum from the mothers of infants suffering from the disease and from adults suffering from various other diseases support the hypothesis of a latent *Pneumocystis* infection in the mother in many cases as the source of infection in the infant. *H. S. Baar*

644. **A Study of Antigenic Relationships in Some Strains of *Corynebacterium diphtheriae***
G. J. HERMANN and E. I. PARSONS. *American Journal of Hygiene* [*Amer. J. Hyg.*] **61**, 64–71, Jan., 1955. 7 refs.

Pharmacology

645. **The Medicinal Use of Placental Extract and Blood.** (Применение порошкообразного препарата плаценты и крови из пуповины (Предварительное сообщение))
A. Bong. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **33**, 73–76, Jan., 1955.

Human placental tissue has been used as a tonic in China for 1,000 years. It is said that a powdered preparation improves appetite, relieves headache, increases sexual function in adult males, and in children promotes an increase in weight and vitality. The author (who writes from Shanghai) has tried the effect of injections of 10 ml. of blood serum from the umbilical vein in cases of arthritis, hypertension, asthma, and diabetes mellitus. In every case it is claimed that the general condition and nutritional status of the patient improved; in some of the cases of arthritis pain was much relieved, while in the asthmatics the attacks were controlled and in some cases ceased. In one diabetic patient the glycosuria disappeared while the injections were being given, only to reappear 6 days after they ceased. Hypertension, however, was but little affected, although the general well-being of the patient was enhanced, giddiness diminished, and insomnia relieved, both by injections of umbilical blood serum and administration of dried placental powder. [Two capsules of the latter were given daily, but the dose in each capsule is not stated.] The clinical histories of 4 cases of polyarthritis, 3 of arthritis of the shoulder, 4 of bronchial asthma, 4 of hypertension, and 2 of diabetes mellitus are briefly outlined.

[It is conceivable that some of the effect is due to the presence of antibodies in placental tissue; these, as well as chorionic gonadotrophin, have been used in prophylaxis in Great Britain.] *L. Firman-Edwards*

646. **Metabolic and Hemodynamic Changes Induced by the Prolonged Administration of Dextran**
J. R. Jaenike and C. Waterhouse. *Circulation* [*Circulation (N.Y.)*] **11**, 1–13, Jan., 1955. 4 figs., 24 refs.

In a study of the effects of large amounts of dextran, carried out at the University of Rochester School of Medicine, New York, preparations of dextran ranging in molecular weight from 25,000 to 185,000 (average 70,000) were given as a 6 or 12% solution in 0·9 or 0·5% saline to 5 male and 2 female patients aged 19 to 58 who showed no evidence of cardiovascular or metabolic disease. The patients were placed on a low-calorie, low-carbohydrate diet in order to produce ketosis and negative nitrogen balance, dietary analyses being performed daily. The dextran was given in daily intravenous infusions to a total of 240 to 720 g. over 2 to 10 days. There were no immediate vasomotor or pyrogenic reactions, but several patients complained of headache some hours after the infusions. The onset of pulmonary congestion in the oldest subject (a negro woman of 58) and of exacerbation of dermatitis in another made it necessary to stop the infusions in these cases; in 4 further patients there was unexplained prolongation of the bleeding time and a haemorrhagic tendency.

During the periods of dextran infusion there was retention of sodium, potassium, and chloride, and all the subjects gained weight, to a maximum of 5 kg. At the end of the various periods of dextran administration the amount of circulating dextran varied from 11·2 to 32·5% of the total dose administered. The amount excreted ranged from 42·5 to 61·1%, and the amount that could not be accounted for varied from 16·0 to 34·8%. In all the subjects the venous haematocrit value fell (average decrease, 23% below control values) and in some it continued to fall in the follow-up period; in no case did it return to its previous level, although in 4 cases the follow-up period was extended to 6 weeks. There was a reduction in the serum protein level by 22 to 53% of the control level, and the total circulating protein level also fell, with one exception; but in the 4 patients who were followed up for 6 weeks there was a subsequent rise in the total protein level above control levels. The maximum serum level of dextran observed was 3·17 g. per 100 ml., but levels above 200 mg. per 100 ml. persisted up to 110 days after the end of the experiment.

There was no evidence of renal damage in the form of proteinuria or reduced renal clearance. The nitrogen-sparing and phosphorus-retaining effects of dextran were demonstrated during the infusion periods and were roughly correlated with the amount of dextran that could not be accounted for by urinary excretion or retention in the blood stream, suggesting that a constant fraction of these calculated amounts of dextran had been metabolized. Acetonuria, which had been demonstrated during the pre-dextran period, diminished during the administration of dextran. The metabolic effect of dextran seemed to differ from that of glucose, but the site and mechanism of its metabolism are still unknown. The authors conclude by drawing attention to the apparent role of plasma proteins in the regulation of blood volume. *K. G. Lowe*

647. **Reserpine Antagonism of Morphine Analgesia in Mice**
J. A. Schneider. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **87**, 614–615, Dec., 1954. 1 fig., 10 refs.

In experiments on mice the effects of reserpine (" serpasil ") and of chlorpromazine on the analgesic action of morphine were studied. The pain threshold was measured by exposing the tails of the mice to a beam of heat and timing the exposure required to produce a flick of the tail. Duplicate readings for each of 10 mice were recorded in each experiment.

The results were as follows. Reserpine alone, in doses up to 10 mg. per kg. body weight given subcutaneously, did not alter the reaction time; chlorpromazine,

10 mg. per kg., prolonged it slightly; and morphine in a similar dose was followed by marked prolongation of the reaction time. Reserpine administered 2 hours before morphine reduced the analgesic effect of morphine in proportion to the dose of reserpine, and chlorpromazine given with morphine prolonged the period of analgesia.

As the author points out, the findings do not indicate the site of action or mechanism of this antagonism or synergism. That chlorpromazine enhances the analgesic effect of narcotic drugs has already been observed in man, and it will be of interest to see if the antagonism exerted by reserpine in mice is also reproduced clinically.

T. B. Begg

648. **A Study of the Action of Tricyclamol Chloride**
P. AYLETT and A. H. DOUTHWAITE. *British Medical Journal* [*Brit. med. J.*] **1**, 691–693, March 19, 1955. 3 figs., 5 refs.

At Guy's Hospital, London, the authors found that an intramuscular injection of 50 mg. of tricyclamol chloride (DL-N-methyl-3-*cyclo*hexyl-3-hydroxy-3-phenylpropyl pyrrolidinium chloride), a new parasympathetic blocking agent, considerably reduced gastric, duodenal, and small-intestinal motility, this effect being observed radiologically after a barium meal. Cholecystography in one patient after intramuscular injection of tricyclamol showed that the gall-bladder emptying time was reduced. In 2 patients given the drug there was a slight reduction in the levels of free and total acid in the gastric contents after a test meal, as compared with control findings.

As is well known, aluminium hydroxide gel reduces the level of free acid in the gastric contents following a gruel meal and delays the peak level of total acid for some 2 hours. When a dose of 100 mg. of tricyclamol was given by mouth these effects were prolonged. Side-effects causing slight discomfort and including dryness of the mouth and dilated pupils were, however, observed in most of the patients [few in number]. *G. B. West*

649. **Anticholinesterases and Muscle Relaxants**
B. G. B. LUCAS and S. MILES. *British Medical Journal* [*Brit. med. J.*] **1**, 579–580, March 5, 1955. 6 refs.

The authors, at the Chemical Defence Experimental Establishment, Porton, Wiltshire, set out to determine whether it might be necessary to modify the dose of certain muscle relaxants when the blood cholinesterase level had been lowered by previous exposure to "sarin" (*iso*propylmethylphosphonofluoridate), an anticholinesterase used as an insecticide. Rhesus monkeys weighing about 4 kg. were anaesthetized with 0·1 g. thiopentone intravenously and connected to a respiratory pump by intratracheal intubation. A pneumograph was attached to the chest, giving a continuous record of respiratory movement. After the relaxant under investigation had been injected, 1 ml. of blood was withdrawn for plasma cholinesterase estimation. At 5-minute intervals the respiratory pump was switched off for 30 seconds to ascertain whether spontaneous respiration had returned. The duration of paralysis was taken as the time elapsing between the injection and the establishment of a respiratory excursion which would lead to survival without further use of the pump. Blood was also withdrawn for cholinesterase estimation at the end of the experiment.

Sarin was injected subcutaneously in a dose sufficient to cause marked miosis, salivation, respiratory distress, and muscular fibrillation. Enough of the relaxants was given to produce respiratory paralysis for 30 to 90 minutes. Cholinesterase was estimated by Ammon's modification of Warburg's manometric method.

The relaxants were tested in pairs: tubocurarine and decamethonium, gallamine and succinylcholine. In 5 monkeys the second member of one pair was injected a week after the first member. Sarin was then administered and the drugs given again in the same order at an interval of a week. In a second group of 5 animals the same pair was tested in the reverse order. Similar tests were carried out on the other pair. No relaxant affected the action of another in any experiment, so that it was possible to consider each agent independently.

With tubocurarine and gallamine there was a significant decrease in the period of respiratory paralysis after sarin, whereas with succinylcholine there was a significant increase. These effects were only temporary. Sarin had no appreciable effect on the respiratory paralysis following decamethonium injection. The results of the cholinesterase estimations were so anomalous that no attempt was made to correlate them with the periods of respiratory paralysis.

The authors point out that these results are in accordance with current theories that tubocurarine and gallamine inhibit acetylcholine at neuromuscular junctions and that this effect is inhibited by sarin. The failure of sarin to affect the action of decamethonium is compatible with the view that decamethonium merely mimics the action of acetylcholine and so is unaffected by anticholinesterase. *Norval Taylor*

650. **The Effect of Sleep and of Stimulation of the Central Nervous System on the Haematopoietic Action of Ferrous Lactate and of Liver Extract.** (Действие молочнокислого железа и камполона на кроветворение на фоне сна и возбуждения центральной нервной системы)

A. Z. TOLOKNEVA. *Фармакология и Токсикология* [*Farmakol. i Toksikol.*] **18**, 28–30, Jan.–Feb., 1955.

In experiments carried out at the Khabarovsk Medical Institute the effect of ferrous lactate and liver extract on the blood picture was studied in rabbits rendered anaemic with phenylhydrazine under various conditions of the central nervous system, that is: (1) the normal state, (2) during depression with barbitone, and (3) during stimulation with caffeine.

The administration of barbitone significantly delayed the response both to iron and to liver extract, whereas that of caffeine produced a significant acceleration of recovery. This effect was also observed in animals recovering spontaneously.

[The author's conclusions regarding the effects of stimulation and depression of the central nervous system on the haematopoietic action of liver extract are hardly justified, since the extract has no specific effect on anaemia of the haemolytic type.] *A. Swan*

Chemotherapy

651. **Studies on the Synergistic Combinations of Drugs**
I. DAVIS and M. G. SEVAG. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **5**, 80–95, Feb., 1955. 3 figs., 30 refs.

Problems of synergism have been studied by the authors at the University of Pennsylvania, Philadelphia. By utilizing two different media—salt–glucose and nutrient broth—they observed 3 different patterns of activity amongst 10 antibacterial drugs tested against 5 species of Gram-negative micro-organism. Regardless of the species of micro-organism, greater resistance to bacitracin, streptomycin, and neomycin was encountered on the salt–glucose medium than on the nutrient broth (Pattern 1), whereas with penicillin, aureomycin, oxytetracycline, chloramphenicol, carbomycin, and sulphathiazole the reverse was found (Pattern 2). With polymyxin B the species of micro-organism appeared to be a factor determining whether Pattern 1 or 2 prevailed (Pattern 3). On the basis of these patterns, certain synergistic and, to some extent, non-synergistic combinations of drugs may be predicted, synergism being more likely if the two drugs show different patterns of activity than if their activity appears to be related to the same enzymatic pattern in the bacterial cell. Experiments providing confirmation of such predictions are described. *A. Ackroyd*

652. **Immunologic Aspects of Penicillin Reactions**
S. S. WINTON and E. D. NORA. *American Journal of Medicine* [*Amer. J. Med.*] **18**, 66–73, Jan., 1955. 42 refs.

Reactions to penicillin therapy, including anaphylaxis and various dermatoses, were observed in 6 cases at Columbus Hospital, Chicago. In the first case, which proved fatal, a woman of 78 was treated with penicillin for a sore throat; 8 days later haemorrhagic bullae developed, associated with fever, leucocytosis, and albuminuria. Pemphigus vulgaris was diagnosed. Treatment with cortisone and ACTH resulted in some improvement, but the lesions became infected and a further course of penicillin was given. More bullae then appeared on fresh sites, but these rapidly resolved when oxytetracycline was administered. A few days later another injection of penicillin was given for thrombophlebitis, and this was followed one hour later by anaphylactic shock and death. At necropsy serous myocarditis, pulmonary oedema, central necrosis of the liver, mild interstitial nephritis, and generalized vascular necrosis were found. Histologically, the bullae showed distended blood vessels, oedematous endothelium, perivascular lymphocytosis, and plasmocytic infiltration.

The main features in the remaining 5 cases were erythema, urticaria and pruritus, joint swelling and pain, and orbital oedema. In one case penicillin had not been administered before; in another penicillin had been given several years earlier and had produced a mild reaction. There was no history of allergic reactions in the patients' families.

It is believed that penicillin links with serum albumin to form a complex capable of participating in an antibody–antigen reaction, and the authors cite the work of Tompsett *et al.* (*J. Bact.*, 1947, **53**, 581; *Abstracts of World Medicine*, 1948, **3**, 238), who found that 50% of penicillins G (benzyl penicillin), X, and F and about 90% of penicillin K so combine with serum albumin. In the present authors' view the anaphylactic-shock type of reaction to penicillin should be treated by repeated intravenous injection of adrenaline or by continuous infusion of noradrenaline together with cortisone and aminophylline. In the serum-sickness type of reaction the antibody–antigen response should be suppressed by administration of adrenaline every 2 to 4 hours, ephedrine, ACTH, and cortisone; in about half the cases there is a mild reaction after the last dose of the cortisone.

The antihistamines were of little value in the present series of cases, but pethedine relieved discomfort. Neostigmine was beneficial in 3 patients who complained of lassitude, extreme fatigue, and general muscular weakness after the allergic reaction. While the cause of this asthenia in the post-allergic state is not yet clear, the authors suggest that neostigmine should be tried in similar cases. They emphasize the importance of preventing these reactions by administering penicillin only when indicated and in the smallest effective dose.
A. Gordon Beckett

653. **The Question of Antagonism between Penicillin and Chlortetracycline, Illustrated by Therapeutical Experiments in Scarlatina**
J. STRÖM. *Antibiotic Medicine* [*Antibiot. Med.*] **1**, 6–12, Jan., 1955. 2 figs., 16 refs.

After considering the conflicting evidence concerning antagonism between various antibiotics the author, in a study carried out at the Hospital for Contagious Diseases, Stockholm, attempted to solve the problem by clinical observation. Three groups, each of 105 patients suffering from uncomplicated scarlatina, were treated respectively as follows: (1) with penicillin, (2) with penicillin and chlortetracycline (aureomycin), and (3) with aureomycin only. The patients in all three groups responded rapidly, the elimination of streptococci from the nose and throat being equally rapid and the outcome similar in all groups. In a follow-up study of these patients, however, it was found that streptococci returned much more frequently in those who had received aureomycin or aureomycin and penicillin. The author concludes that these two antibiotics may be antagonistic, that aureomycin had impaired the effect of penicillin, and that the treatment of scarlatina with aureomycin, either alone or in combination with penicillin, is contraindicated. *I. A. B. Cathie*

654. **Influence of Deoxycortone and Cortisone on the Blood Level of Long-acting Penicillin.** (Zum Einfluss von Desoxycorticosteron und Cortison auf den Blutspiegel eines Depotpenicillins)
G. STÜTTGEN. *Zeitschrift für Haut- und Geschlechtskrankheiten* [*Z. Haut- u. GeschlKr.*] **18**, 97–99, Feb. 15, 1955. 3 figs., 9 refs.

At Düsseldorf Medical Academy patients receiving 100 mg. of cortisone daily and 12 controls were given an intramuscular injection of 600,000 units of " tardocillin compound ", a preparation consisting of equal parts of procaine penicillin and benzathine penicillin. The concentration of penicillin in the blood was determined 24, 48, and 72 hours later, and was slightly lower in the patients receiving cortisone than in the control group; it was below the critical therapeutic level (taken as 0·03 unit per ml.) in only one of the control subjects at 72 hours compared with 5 of those having cortisone as well. A further 11 patients who were receiving 5 mg. of deoxycortone acetate intramuscularly daily were given a similar dose of tardocillin and showed a far more rapid fall in the blood level of penicillin than those receiving cortisone, none of them maintaining a critical therapeutic level for as long as 72 hours. Experiments *in vitro* showed no inactivation of penicillin by the two hormones, and as the blood levels of penicillin were low throughout the test period the initial absorption of penicillin did not appear to be increased by the hormones. A possible explanation may be found in increased diffusion of the penicillin into the tissues from the circulation or increased renal elimination under hormonal influence. *G. W. Csonka*

655. **A Comparison of the Antirickettsial Action of " 5337 RP " or " Spiramycin " with that of Aureomycin and of Oxytetracycline (" Terramycin ").** (Comparaison de l'action anti-rickettsienne du 5337 RP ou spiramycine avec celle de l'auréomycine et de la terramycine)
P. GIROUD. *Bulletin de la Société de pathologie exotique et de ses filiales* [*Bull. Soc. Path. exot.*] **47**, 642–644, Oct. 13, 1954. 1 fig.

The author points out that in comparing the action of substances used in the treatment of rickettsioses the toxic effect of the drug on the experimental animal must be taken into account as well as that on the micro-organism and for this reason rabbits are more suitable than mice. The author's technique is to inject various doses of rickettsial material [species not stated] intradermally into rabbits, the nodules which develop being measured volumetrically over a period of 3 to 11 days. Treatment is started on the first day or later, and its effect on the size of the nodules observed by plotting the volumetric measurements on a graph. Examples of experimental results obtained by this method are quoted in which the effects of equivalent doses of " 5337 RP " (" spiramycin "), aureomycin, and " terramycin " (oxytetracycline) were compared. It was concluded that spiramycin acts successfully against the rickettsiae used, and is of relatively low toxicity.

[For full details of the technique readers are referred to a previous paper by the author (*Bull. Soc. Path. exot.*, 1942, **35**, 345).] *B. G. Maegraith*

656. **Streptomycin–Oxytetracycline Combined Therapy: Correlation between *in vivo* and *in vitro* Trials**
E. M. SWANTON, H. E. LIND, and E. H. BEUTNER. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **5**, 124–128, March, 1955. 4 refs.

Eleven strains of Gram-negative bacilli associated with chronic urinary tract infections were repeatedly assayed for their *in vitro* sensitivities to oxytetracycline, streptomycin, and a combination of these two by the disc plate and serial tube dilution technics. Results of each method agreed with streptomycin and oxytetracycline. The methods failed to agree in 2 cases using the combination. Combined streptomycin–oxytetracycline therapy and streptomycin therapy alone correlated with *in vitro* findings. There was very poor correlation with oxytetracycline. No cases of synergism or antagonism were demonstrated. Clinically, combined streptomycin–oxytetracycline therapy demonstrated a response similar to that of streptomycin alone.—[Authors' summary.]

657. **The Sensitivity of *Salmonella typhi* to Synnematin B and Other Antibiotics. A Study of Forty Freshly Isolated Strains**
J. OLARTE and G. FIGUEREDO. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **5**, 162–165, March, 1955. 1 fig., 5 refs.

The action of " synnematin B " [isolated from mould cultures of *Cephalosporium salmosynnematum*], chloramphenicol, and tetracycline antibiotics was studied on 40 freshly isolated strains of *S. typhi*. Comparable results were obtained with the tube dilution and the agar dilution methods. High sensitivity was obtained to the five antibiotics, synnematin B being the most active. The order of diminishing activity was: synnematin B, tetracycline, oxytetracycline, chloramphenicol, and chlortetracycline. The sensitivity of the 40 strains of *S. typhi* studied was uniform within a narrow range.—[Authors' summary.]

658. **Preliminary Study of Treatment with Neomycin of Diarrhea Caused by *Shigella* and *Salmonella***
E. PONCE DE LEÓN. *Antibiotic Medicine* [*Antibiot. Med.*] **1**, 20–22, Jan., 1955. 3 refs.

In this report from the clinic of the Institute of Social Security, Mexico City, the author describes the cases of 25 children under 2 years of age suffering from intestinal disorder and diarrhoea, in 15 cases due to infection with *Salmonella* and in 10 with *Shigella*, who were treated with neomycin in a dosage of 50 mg. per kg. body weight per day, divided into equal 4-hourly doses, for 5 days. Treatment was instituted early, in no case later than the third or fourth day of the illness. All but 4 of the patients were cured clinically and bacteriologically, vomiting diminishing first, then pain, and finally temperature and the number of stools; it was noted that the general condition of the child on admission was important in determining the rapidity of clinical response. In the 4 cases of failure (that is, no clinical improvement in the first 4 days of treatment), one was due to infection with *Salmonella typhosa*, 2 with *Shigella dysenteriae*, and one with *Sh. alkalescens*. The drug caused no undesirable side-effects. *I. A. B. Cathie*

Infectious Diseases

659. **Human Infection with Pleuropneumonia-like Organisms**
E. J. STOKES. *Lancet* [*Lancet*] **1**, 276–279, Feb. 5, 1955.

In this paper from University College Hospital, London, a method for the isolation of pleuropneumonia-like organisms (PPLO) and the preparation of antigen for serological diagnosis are first described. The organisms were grown on modified Nagler's medium, which had previously been flooded with penicillin or erythromycin or incorporated thallium acetate. Swabs were not allowed to dry before cultures were prepared. Minute colonies appeared after 3 days' incubation and were examined in an impression preparation, because the usual films made from scraped colonies showed no recognizable structures. Satisfactory antigens for agglutination tests were difficult to prepare, but antigen for complement-fixation reactions was made by centrifuging human plasma broth cultures and resuspending the deposit in saline solution. The antigen was used untreated, since killing the organisms by heat at 56° C. rendered the suspension anticomplementary. For antisera rabbits were injected intravenously with an antigen similarly prepared, except that rabbit serum broth was used as the culture medium.

The author then describes 4 cases of infection with PPLO. In 2 there was post-partum pyrexia, and PPLO were cultured from the blood in one case and from a high vaginal swab in the other. In the third case these organisms were isolated from a bronchopleural fistula which had developed after lobectomy for bronchiectasis. In the fourth case there was a long history of abdominal sepsis and PPLO were isolated from a high vaginal swab. Administration of aureomycin (but not penicillin) was followed by clinical improvement in 3 cases. Complement-fixing antibody titres were low in one case but reached significant levels in 3; the titres were highest at about 3 weeks. The results of control tests carried out on 172 specimens of serum were negative in all except one instance.

The author considers that although Koch's postulates cannot be applied to PPLO, there is good evidence for regarding the cases described as examples of infection with these organisms. *R. B. Lucas*

660. ***L. canicola* Infection Treated by Penicillin**
J. CROOKS and W. BLAIR. *British Medical Journal* [*Brit. med. J.*] **1**, 885–887, April 9, 1955. 20 refs.

Two cases of human infection with *Leptospira canicola* are described. *L. canicola* infection should be considered in the differential diagnosis of unexplained pyrexia or lymphocytic meningitis. Evidence is produced to show that the incubation period of the disease is about 7 days and that the early administration of penicillin in high dosage is an effective form of therapy.—[Authors' summary.]

661. **Aseptic Meningitis: Isolation of Coxsackie and Unidentified Cytopathogenic Viruses from Cerebrospinal Fluid by Tissue Culture Methods**
D. DUNCAN, A. J. RHODES, G. A. MCNAUGHTON, C. C. R. JOHNSON, and W. WOOD. *Canadian Journal of Public Health* [*Canad. J. publ. Hlth*] **46**, 1–8, Jan., 1955. 14 refs.

Coxsackie viruses and another unidentified agent have been isolated from the stored cerebrospinal fluid of patients who developed benign aseptic meningitis during an epidemic in Toronto in 1952. Cytopathological changes were noted in tissue cultures from monkey kidney treated with trypsin which had been inoculated with cerebrospinal fluid from 6 of the 52 patients concerned (see *Canad. J. publ. Hlth*, 1954, **44**, 55). As a result of further detailed studies by animal inoculation of infected tissue-culture fluid and by serological tests for homologous antibodies carried out at the University of Toronto 3 of the agents have been identified as Group-B Coxsackie viruses. Since the fluids had been inoculated 2 years previously in suckling mice without producing signs of illness, the value of the simple technique of tissue culture in the primary isolation of the Coxsackie viruses is underlined.

Another 2 agents, presumably viral, remain unidentified " orphan " viruses. They were not pathogenic for suckling mice or rhesus monkeys, but they were associated with a significant rise in homologous serum antibody level.

The cytopathogenic agents were not neutralized by poliomyelitis antisera, but were all neutralized by commercial gamma globulin. *D. Geraint James*

662. **Medical Management of the Long-term Respirator Patient**
H. N. NEU and H. A. LADWIG. *Journal of Chronic Diseases* [*J. chron. Dis.*] **1**, 160–167, Feb., 1955. 3 figs., 7 refs.

663. **Upper Gastrointestinal Lesions in Acute Bulbar Poliomyelitis**
A. SCHABERG, J. A. HILDES, and A. J. W. ALCOCK. *Gastroenterology* [*Gastroenterology*] **27**, 838–848, Dec., 1954. 4 figs., 27 refs.

Lesions of the upper gastrointestinal tract were encountered in 62 out of 1,175 cases of poliomyelitis admitted to the Winnipeg Municipal Hospitals during the epidemic of this disease in 1953. These lesions were found only in cases of bulbar poliomyelitis, the total number of which was 480. In 34 of the 62 cases there was clinical evidence of gross haemorrhage. Necropsy in the remaining cases revealed gross duodenal erosions in 9 cases (with perforation in 3), small erosions in 17, and rupture of the oesophagus in 2. The histological appearances were characteristic, and consisted in dilata-

tion of the capillaries and sometimes also of the arterioles, with occasional thrombus formation and infarction. While the brain stem was affected in all cases, this was by no means true of the hypothalamus. The authors therefore do not concur in the view that gastrointestinal erosions are associated only with hypothalamic lesions. They believe that the mechanism differs from that in peptic ulceration since their patients with gastrointestinal complications included 4 pregnant women who, as is well known, are resistant to spontaneous ulceration.

R. Schneider

664. **Use of Gamma Globulin for Control of Infectious Hepatitis in an Institution for the Mentally Retarded**

A. ASHLEY. *New England Journal of Medicine* [*New Engl. J. Med.*] **252**, 88–91, Jan. 20, 1955. 1 fig.

An outbreak of infective hepatitis in a State institution for the mentally retarded in Maine was apparently rapidly terminated by the mass inoculation of the inmates and staff with gamma globulin in a dosage of 0·01 ml. per lb. (0·02 ml. per kg.) body weight. The institution accommodated some 1,500 patients and 233 staff, but owing to discharges and admissions the attack rate could not be accurately calculated. Inoculations of gamma globulin were given to 145 members of the staff and 754 inmates. Of the total staff, 5 who had not been inoculated developed infective hepatitis. There were 152 cases of hepatitis among the patients; of these, 26 occurred in those who had received gamma globulin, jaundice developing less than 5 days after inoculation in 11 and 9 to 31 days after inoculation in the remainder. The outbreak terminated rapidly after the mass inoculations were carried out. *J. E. M. Whitehead*

665. **A Case of Sarcoidosis and Three Cases of Atypical Tuberculosis in a Family**

D. VAN ZWANENBERG and M. BARRY. *Lancet* [*Lancet*] **1**, 483–485, March 5, 1955. 1 fig., 12 refs.

This is a report from the Ipswich Chest Clinic of the occurrence of sarcoidosis in 4 siblings of one family, the other 3 members of which were not examined. The affected members were 3 brothers and a sister, all in the third decade of life. Lymphadenopathy was present in all 4 patients, affecting the axillary or cervical lymph nodes in the 3 males but restricted to the hilar nodes in the female. Confirmatory histological evidence was obtained by biopsy of one of these nodes in each of the brothers and by liver biopsy in the sister. Chest radiographs revealed bilateral scattered pulmonary shadows in one case and hilar adenopathy in 2; in the other case the appearances were normal. In 2 of the patients a negative reaction was obtained to 100 units of tuberculin and in another a negative reaction to 10 units, while in the fourth case there was a positive reaction to 100 units. Following B.C.G. vaccination one of the Mantoux-negative brothers failed to react subsequently to 100 units of tuberculin.

Three of the cases were labelled "atypical tuberculosis" because of the suspicion of central caseation in the histological sections, although acid-fast bacilli were not found. The authors suggest that if a tuberculous aetiology is accepted, then the lesions may represent transitional types between one form of sarcoidosis and tuberculosis. Only in one case was there any suggestion of response to antituberculosis chemotherapy.

D. Geraint James

666. **Kveim Test in Sarcoidosis and Tuberculosis. Preliminary Report**

M. SONES, H. L. ISRAEL, R. KRAIN, and H. BEERMAN. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **24**, 353–364, March, 1955. 4 figs., 13 refs.

Failure to diagnose sarcoidosis by the response to the Kveim test is reported from the Women's Medical College and the University of Pennsylvania, Philadelphia. With the antigen used a positive reaction was obtained in about one-third of the patients with sarcoidosis, in two-fifths of those with tuberculosis, and in 2 control subjects. However, when the antigen was passed through coarse and ultra-fine sintered glass filters, the non-specific positive reactions in patients with tuberculosis were abolished. Furthermore, when antigens from other laboratories were used, there were no false positive results in the patients with tuberculosis.

The authors are at a loss to explain the results, which are clearly at variance with those of other workers and those obtained with antigens supplied to them from other sources. They discuss in detail some of the possible causes of failure, and question the accuracy of their histological differentiation of sarcoid tissue from a foreign-body granuloma.

[The false positive sarcoid reactions occurred only with one batch of antigen, and these were abolished when the antigen was filtered. The presence of tubercle bacilli in the unfiltered antigen could account for the non-specific sarcoid reactions; the authors do not discuss this. It would appear that tubercle bacilli were not sought by culture or guinea-pig inoculation of the material used in the preparation of the antigen.]

D. Geraint James

667. **Treatment of Pulmonary Sarcoidosis with Streptomycin and Cortisone**

C. HOYLE, J. DAWSON, and G. MATHER. *Lancet* [*Lancet*] **1**, 638–643, March 26, 1955. 7 figs., 20 refs.

A selected group of 38 patients with pulmonary sarcoidosis at King's College and Brompton Hospitals, London, were treated with streptomycin and PAS (30 patients) and with cortisone in addition (20 patients); the latter group included 12 patients who had previously failed to respond to streptomycin and PAS alone. The results of treatment were judged mainly by the degree of improvement in the chest radiographs, and were analysed in relation to the approximate duration of the disease.

In the group given streptomycin and PAS improvement was noted in 11 out of 21 patients in whom the disease had been present for less than 2 years but in only one out of 9 in whom the duration was more than 2 years. Of the patients given cortisone in addition to streptomycin and PAS, 11 had had the disease for more than 2 years and 8 of these were improved; of the remaining 9 patients in whom the duration was less than 2 years, all improved.

D. Geraint James

Tuberculosis

668. **Primary Miliary Infection of the Newborn. Pulmonary Tuberculosis due to Aspiration of Amniotic Fluid.** (La miliaire primaire du nouveau-né. Tuberculose pulmonaire par aspiration amniotique)
M. LELONG, A. ROSSIER, LE TAN VINH, and G. GUYON. *Archives françaises de pédiatrie* [*Arch. franç. Pédiat.*] **12**, 1–19, 1955. 7 figs., 19 refs.

The authors quote 11 cases from the literature and describe 3 cases of their own in which primary miliary tuberculosis in a newborn baby was due to aspiration of amniotic fluid during labour or to post-natal inhalation. The initial signs appear in the majority of cases between the 15th and 20th days and consist in a rise of temperature to 38° or 38·5° C. (100·4° to 101·3° F.), loss of weight, dyspnoea with cyanosis, and inconstant rales heard over the lungs. The reaction to tuberculin is negative. In the radiograph of the chest disseminated miliary foci are visible, and histological examination of the lungs reveals small pneumonic foci, the alveolar ducts being filled with necrotic material containing numerous tubercle bacilli.

In the authors' cases the babies died on the 23rd, 24th, and 29th days respectively. The lung changes described above were present, but all other organs were found to be free from tuberculosis. One mother had bilateral pulmonary tuberculosis associated with ulceration of the mouth, the second had active tuberculosis during pregnancy but the lesions were healed at the time of delivery, and the third mother was suffering from tuberculous endometritis, a disease which is very often latent and without any disturbing effect on the mother.

Franz Heimann

DIAGNOSIS AND PROPHYLAXIS

669. **A Clinical, Radiological, and Tuberculin Survey 10 to 14 Years after Vaccination with Petragnani's Integral Anatuberculin.** (Un tentativo di controllo clinico, radiologico e tubercolinico a 10–14 anni di distanza dalla vaccinazione con Anatubercolina Integrale Petragnani (AIP))
L. F. SIGNORINI and C. PANERO. *Clinica pediatrica* [*Clin. pediat. (Bologna)*] **36**, 899–910, Dec., 1954. 27 refs.

The authors, writing from the Institute of Hygiene of the University of Florence, describe a survey of a number of persons who had been tuberculin-negative 10 to 14 years previously and had then been vaccinated with Petragnani's " integral anatuberculin " (a preparation of formol-killed tubercle bacilli), and of a comparable group of unvaccinated control subjects. Out of 1,293 persons originally vaccinated, 368 were followed up. Of these, 2 had died of tuberculosis (mortality 0·54%) and 10 of other causes; of 174 who were examined in detail, 15 (8·62%) showed radiographic evidence of old or recent tuberculous disease and 81·1% gave a positive tuberculin reaction. Of the control group, consisting of 137 unvaccinated persons, all brothers of members of the vaccinated group, 6 had died of tuberculosis (mortality 4·38%), while of 66 studied in detail, 16 (24·24%) had radiological evidence of old or recent disease and 66·67% were tuberculin-positive. The authors conclude that the vaccine has some protective value and that its effect may persist in a high proportion of cases for at least 10 years. They recognize, however, that the ultimate evaluation of vaccine requires a very much larger and more extensive survey.

Reactions after vaccination consisted usually in moderately intense local phenomena, but in 40% of cases ulceration developed; this usually healed quickly, though in 4 cases Koch's phenomenon occurred, with severe local ulceration and associated lymphadenopathy which subsided eventually.

Arnold Pines

670. **The Reaction of Di Maria in Infantile Tuberculosis.** (Considerazioni sulla reazione del Di Maria nella tubercolosi infantile)
E. SEGAGNI and G. BONO. *Minerva pediatrica* [*Minerva pediat. (Torino)*] **7**, 190–199, Feb. 17, 1955. 17 refs.

The reaction developed by Di Maria at the Forlanini Institute, Rome, consists in the precipitation by an alcoholic solution of mercuric chloride of certain globulin fractions present in excess in the serum in tuberculosis. It is claimed to be the most accurate and useful of the many similar tests (such as those of Takata, Gros, Kunkel, and Ucko) sometimes employed in the study of tuberculosis.

To perform the test, 0·7 ml. of 1% mercuric chloride solution and 0·3 ml. of 95% alcohol are well mixed and 0·04 ml. of unhaemolysed serum then added. Often there is an immediate reaction, floccules of large, medium, or small size forming. Sometimes the mixture merely becomes turbid at first, floccules of varying size forming later. The time taken for flocculation and the size of the floccules indicate the degree of toxicity or activity of the disease: thus immediate flocculation indicates a very high degree of toxicity, while the formation of small floccules in 5 to 10 minutes indicates only slight activity. Flocculation occurring after 10 minutes is believed to show that the lesions are quiescent, and may be a non-specific reaction.

The present authors have performed the test on serum from 129 children at the Queen Margherita Children's Hospital, Turin, 37 of whom had tuberculous lymphadenopathy (including mediastinal), 24 recent exudative pulmonary tuberculous disease, and 88 tuberculous meningitis, while the remaining 60 were suffering from non-tuberculous disease or were healthy. The erythrocyte sedimentation rate (E.S.R.) was also determined in each case. In the tuberculous cases there was a close correlation between the intensity of Di Maria's reaction and the E.S.R. [though not in all cases]. This was parti-

cularly marked in cases of exudative meningeal infection, the results of both tests being closely related to the clinical state. In the control subjects the reaction was positive in only a few cases of varying aetiology—especially in one case of hepatitis and two cases of lipoid nephrosis. The authors conclude that the reaction is of much value in the diagnosis and prognosis of tuberculosis in childhood.

[In no case was the reaction repeated during the course of the illness as an index of response to treatment or to determine when a quiescent state had been reached. This appeared to the abstracter to be the most valuable application of the test when he recently saw it in use in Di Maria's department at the Forlanini Institute. It sometimes appeared to give more exact information than the E.S.R. in these respects.] *Arnold Pines*

RESPIRATORY TUBERCULOSIS

671. **Bronchoscopy of the Tuberculous**
G. R. McNab. *Tubercle* [*Tubercle* (*Lond.*)] **36**, 55–58, Feb., 1955. 19 refs.

In this paper are analysed 250 bronchoscopies performed on tuberculous patients at Foxhall Hospital, Ipswich. The technique is as follows. "Omnopon" and scopolamine are used as premedication, and the patient sucks a 100-mg. tablet of amethocaine 15 minutes before the examination. Local analgesia is employed, 2% amethocaine being applied to the pyriform sinuses and 2 ml. being dropped into the larynx through the nose. With the head extended and the neck flexed the bronchoscope is passed direct, or through a laryngoscope if there is any difficulty. Additional local analgesic is applied with a Robert spray, and secretions are removed by swabbing, not by suction. The bronchial tree is finally cleared by suction, and the patient lies on the affected side after the examination. Indications include radiological evidence of segmental or lobar distribution of lesions, tension and multiple cavities, clinical evidence of obstruction, haemoptyses or positive sputum of uncertain origin, postoperative atelectasis, and cases where carcinoma must be excluded; it is also used as a preliminary measure to collapse therapy or resection. The author's criteria for the diagnosis of tuberculous endobronchitis are the presence of ulceration, granulation tissue, or fibrostenosis. He notes that the examination may reveal bronchial spasm, obstruction, or distortion, a source of bleeding, or the presence of a perforating lymph node, and that specimens of sputum or swabs may be taken and bronchospirometry carried out.

The only complication in this series was tuberculous laryngitis in one case. All "wet" bronchoscopies were followed by the use of chemotherapy.

Bronchoscopic abnormalities were noted 147 times, although in only 37 instances were the changes specific for tuberculosis. The possible source of a positive sputum was seen on 24 occasions, but only 9 positive cultures were obtained from swabs. The author uses a protected swab to prevent contamination from the opposite side. *L. Capper*

672. **A Comparison of the Clinical, Radiological, and Bacteriological Results of Ten Months' Treatment of Pulmonary Tuberculosis with Isoniazid Combined with PAS and with Streptomycin.** (Comparaison des résultats radiocliniques et bactériologiques du traitement continu pendant dix mois de la tuberculose ulcéro-nodulaire par les associations I.N.H.-P.A.S. et I.N.H.-streptomycine)
P. Véran. *Revue de la tuberculose* [*Rev. Tuberc.* (*Paris*)] **18**, 1153–1172, 1954. 4 figs., 16 refs.

This report records the author's experience in the treatment of advanced, open pulmonary tuberculosis with two pairs of chemotherapeutic agents, each of which was given for periods up to 10 months. The conclusion, after 78 patients had been treated with isoniazid and PAS and 87 with streptomycin and isoniazid, was that there was nothing to choose between the two combinations initially, but that over a longer period those patients treated with streptomycin and isoniazid did slightly the better. Few cases of drug resistance were encountered in either group. There were 17 cases in which the patient's condition deteriorated during treatment after initial improvement, all of them cases of long-standing disease with persistent cavities.

[Unfortunately the author's conclusions, though agreeing with general experience, are based on inadequate grounds, as only 25 members of one group and 16 of the other were examined after 10 months' treatment.] *J. Robertson Sinton*

673. **Tuberculous Pleural Effusions Treated with Streptomycin, *para*-Aminosalicylic Acid, and Early Aspiration**
P. A. Emerson. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **24**, 61–76, Jan., 1955. 1 fig., bibliography.

The author, at the Brompton Hospital, London, compared the results in 25 cases of tuberculous pleural effusion in young adults treated with streptomycin plus PAS combined with rest with those obtained in 40 clinically comparable cases treated with rest only. Of the first group, 19 were also subjected to early aspiration, but this practice was discontinued because of frequent recurrence of fluid, sometimes with increased pyrexia. In both groups most of the effusions were comparatively large, but only about one-fifth of the patients in either group had any signs of parenchymal disease, and with one exception these were minimal.

All patients were strictly confined to bed for at least 3 months. For those receiving streptomycin various schedules of dosage were employed, but the basic principle was to give 1 g. intramuscularly each day at first, reducing this to 1 g. every third day when therapeutic control had been obtained. PAS was given orally in divided doses totalling 15 to 20 g. daily for the duration of the streptomycin course. All the patients have been followed up for at least one year, and most of them for much longer.

The most striking difference was seen in regard to the duration of pyrexia, the mean for this in the streptomycin-treated group being 22 days, as compared with 45 days in the control group. Most of the effusions cleared ultimately, but the clearance times varied greatly

and, in the author's opinion, could not with any certainty be related to treatment. Among patients followed up for 2 years or more, active tuberculosis developed in 9 (22·5%) of the 40 controls, but in only one (4·8%) out of 21 so followed up in the streptomycin-treated group. The author concludes [reasonably, in the abstracter's opinion] that antibacterial therapy is advantageous in the treatment of tuberculous effusion.

R. J. Matthews

674. **The Treatment of Pulmonary Tuberculosis with Intravenous PAS-infusions**
F. CHARLES. *Tubercle* [*Tubercle* (*Lond.*)] **36**, 40–42, Feb., 1955. 8 refs.

The author describes the treatment of 50 patients with intravenous PAS at the Parksanatorium, Davos-Platz, Switzerland. The series included 13 males and 37 females, their ages ranging from 18 to over 60 years. The only complications in 2,235 infusions were one case of allergy and one of thrombophlebitis, both of which cleared up rapidly so that treatment could be continued. Serum sodium and potassium levels were not affected, but there was a constant prothrombin depression reversible by vitamin K, an ampoule of which was therefore added to each infusion bottle. An ordinary blood-transfusion type of apparatus was used for the infusion, but the glass employed had a low alkali content and the parts of the stoppers coming into contact with the solution were varnished. The solution was prepared by adding 5 mEq. of potassium to fresh 5% sodium PAS solution, 500 ml. of this mixture corresponding to 25 g. of sodium PAS or to 18 g. of the free acid. Sterilization was by filtration and not by heat. Treatment consisted in 3 infusions per week for 4 months or more, each taking 1½ to 2 hours. Isoniazid was usually administered concurrently. The absolute indications for this treatment are given as miliary meningeal tuberculosis and pneumonic and endobronchial disease, relative indications including bronchogenic or haematogenous spread, pre- and post-operative care, and resistance to streptomycin and isoniazid.

The author claims that in recent cases of haematogenous disease radiological improvement started after 2 weeks. Permanent cavity closure was obtained in one-third of the cases, while in the remainder the cavities decreased in size. All cases of endobronchial disease improved, but " spreads " did not begin to clear before 2 months. The clinical response was marked, cough and sputum decreasing and the erythrocyte sedimentation rate falling.

L. Capper

675. **The Coordination of Surgery and Combined Chemotherapy in the Treatment of Pulmonary Tuberculosis**
A. M. DECKER, J. W. RALEIGH, and E. S. WELLES. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **29**, 151–162, Feb., 1955. 3 figs., 3 refs.

The authors discuss the results of chemotherapy or chemotherapy and resection in 179 cases of pulmonary tuberculosis with cavitation and positive sputum. All the patients received continuous chemotherapy for 8 months, and at the end of this period 77% were sputum-negative. The patients were then grouped as follows: (1) sputum-negative with closed cavities, 35%; (2) sputum-negative with cavitation, 42%; and (3) sputum-positive with cavitation, 23%; at the end of a year only 11% were in this last group. The authors point out that failure to convert sputum is always associated with open cavities. A high proportion of the patients in Group 2 relapsed within a short period of cessation of chemotherapy, whereas less than 5% of those in Group 1 relapsed whether resection was carried out or not. The results of resection in Group 2 were good, and it is considered that operation is indicated in these cases. In Group 1 the similarity in the results whether resection was carried out or not suggests that operation is much less certainly necessary in these cases. The authors consider that since sputum conversion occurs in many cases within the first 3 months and the risk of the emergence of resistant organisms is greater where cavities remain patent, surgery in cases of positive sputum with cavitation should not be too long delayed; thoracoplasty or other collapse measures should be undertaken in these cases.

J. R. Belcher

676. **The Role of Pulmonary Insufficiency in Mortality and Invalidism following Surgery for Pulmonary Tuberculosis**
E. A. GAENSLER, D. W. CUGELL, I. LINDGREN, J. M. VERSTRAETEN, S. S. SMITH, and J. W. STRIEDER. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **29**, 163–187, Feb., 1955. 12 figs., 30 refs.

The authors have undertaken an extensive pre- and post-operative study of pulmonary function in 460 patients subjected to surgical treatment for advanced pulmonary tuberculosis at the Boston City Hospital since 1947. They endeavoured to keep the tests fairly simple so that they might be performed as a routine. It was found that one-third of the operative deaths (within 30 days) and a similar proportion of the late deaths were due to pulmonary insufficiency. In all cases of operative death the vital capacity was below 2 litres, maximum breathing capacity below 50%, and the " walking dyspnoea index " above 35%.

The dyspnoea which occurred in many cases after surgical treatment was related to the type of operation performed and the degree of respiratory disability present before operation. Disability after operation in excess of that anticipated was due to some accident at the time of the operation, such as haemothorax or pneumothorax, or, at a later stage, to extension of the disease process.

J. R. Belcher

677. **The Clinicopathologic Significance of the Demonstration of Viable Tubercle Bacilli in Resected Lesions**
O. AUERBACH, G. L. HOBBY, M. J. SMALL, T. F. LENERT, and J. V. COMER. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **29**, 109–135, Feb., 1955. 4 figs., 28 refs.

After reviewing the relevant literature the authors describe a study undertaken at the Veterans Administration Hospital, East Orange, New Jersey, in an attempt to correlate the anatomical findings with the viability of tubercle bacilli in resected lesions from patients who had had extensive chemotherapy and who had been culture-

negative for several months. Using special cultural methods [see *Amer. Rev. Tuberc.*, 1954, **70**, 191; *Abstracts of World Medicine*, 1955, **17**, 265] they studied necrotic fragments from resected specimens of lung from 40 tuberculous patients, only 19 of whom are dealt with in this report. Of these 19 patients, 14 had received from 4 to 12 months' chemotherapy and showed evidence of cavity closure, while one had received chemotherapy for 11 months but had evidence of a healed open cavity; the remaining 4 patients, who had either had no previous chemotherapy or had an open cavity at the time of resection, were used as controls. Eleven of the 15 treated cases were under treatment for the first time and the sputum cultures had been positive in 7 of them, while positive sputum had been obtained from all 4 " re-treated " cases. Tubercle bacilli were cultured from lung fragments from all 4 of the control cases and from 11 of the 15 treated cases. On subculture all these strains of bacilli were lethal to guinea-pigs.

Most of the patients had been given streptomycin twice weekly with PAS daily, but some had received daily isoniazid with streptomycin or PAS. However, the limited data available failed to suggest that the particular antibiotic regimen had any effect on the chance of recovering tubercle bacilli from the resected lesions, nor was any correlation found between the duration of antibiotic treatment before operation and the presence or absence of tubercle bacilli in the resected specimens.

On the basis of their findings the authors consider that chemotherapy should not be stopped until all open cavities are resected; also that an inspissated cavity with a communicating bronchus through which its contents can be discharged into the bronchial tree is a potential danger even when the patient has received prolonged chemotherapy. *G. M. Little*

678. **Results of Endocavitary Aspiration Combined with Surgical Collapse Therapy over an 8-year Period.** (Risultati conseguiti dall'aspirazione endocavitaria associata ad interventi collassoterapici nel corso di 8 anni)
D. Parmeggiani and U. de Ascentis. *Archivio di tisiologia* [*Arch. Tisiol.*] **9**, 918–940, Dec., 1954. 10 figs., 1 ref.

The results of cavity drainage of the Monaldi type in 204 cases of pulmonary tuberculosis treated at the Sacco Sanatorium at Milan and at the Tuberculosis Clinic of the University of Naples during the period 1946–53 are described. It is claimed that all cases have been followed up until recently [though no precise periods are stated]. The majority were examples of giant cavitation.

The cases are divided into five clinical groups. (1) In 40 cases drainage resulted in the complete disappearance of the cavity or its reduction to small proportions. Here usually a small " insurance " thoracoplasty was enough to ensure permanent stability, and the drainage tube could usually be removed a few days after operation. In all these cases permanent closure of the cavity was secured. (2) In 3 similar cases cavitation was permanently controlled with the aid of section of the phrenic nerve. (3) In 82 cases drainage brought about some diminution of cavitation, but not complete closure, and here a much more formal and extensive thoracoplasty was necessary. Usually mechanical factors due to the extensive fibrosis of advanced disease were responsible for the limited results of drainage, which nevertheless appeared instrumental in enabling a safer, less extensive, and more successful operation to be performed, though drainage had to be maintained for long periods after operation in some cases to ensure cavity closure. In 58 of these cases the cavity remained permanently closed, in 17 it persisted, and the remaining 7 patients died. (4) In 53 cases cavities had persisted after thoracoplasty and drainage was instituted subsequently. In 35 cases the cavities disappeared permanently, the condition usually being stabilized by a further stage of thoracoplasty, and in 14 the cavities persisted, while 4 patients died. (5) In 26 cases various other procedures were combined with drainage, often in the presence of bilateral cavitation. In 20 cases the treated cavity closed and in 3 it persisted; 3 patients died. Of the total of 204 cases, cavitation was permanently controlled in 156 and persisted in 34, while 14 patients died.

The total period of drainage necessary is defined only in relation to 10 illustrative cases, in which it varied from 3 to 12 months. Persistence or re-opening of the drainage track is considered to be rare since the introduction of chemotherapy. In fact, 10 cases are described in which posterior thoracoplasty was performed in the presence of drainage tubes situated posteriorly, all without incident. *Arnold Pines*

679. **Osteoplastic Thoracoplasty**
R. Brock. *Thorax* [*Thorax*] **10**, 1–8, March, 1955. 18 figs., 4 refs.

680. **Carcinoma of Bronchus in Association with Active Pulmonary Tuberculosis**
A. Sakula. *British Medical Journal* [*Brit. med. J.*] **1**, 759–762, March 26, 1955. 22 refs.

That Rokitansky was probably wrong when he propounded his theory of antagonism between cancer and tuberculosis is suggested by the increasing numbers of cases reported in which both pathological processes have been found together. Of 6 such cases described by the author from the Kingston Chest Clinic, Surrey, 5 presented as cases of tuberculosis and one as a case of carcinoma of the bronchus, tubercle bacilli being demonstrated later. The diagnosis of malignancy was suggested by persistent pain in the chest, lack of response to chemotherapy, and the presence of hilar shadows on the radiograph and of an irregularly walled cavity as seen on tomography. None of the 6 patients was fit for any curative treatment. *J. Robertson Sinton*

681. **A Psychosomatic Study of the Course of Pulmonary Tuberculosis**
E. D. Wittkower, H. B. Durost, and W. A. R. Laing. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **71**, 201–219, Feb., 1955. 14 refs.

See also Pathology, Abstracts 619–20.

Venereal Diseases

682. **Test for Immobilization of *Treponema pallidum*. Correlation with Some of the Standard Serologic Tests for Syphilis**

D. J. MACPHERSON, R. K. LEDBETTER, and V. E. MARTENS. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **25**, 89–92, Jan., 1955. 18 refs.

Treponemal immobilization (T.P.I.) tests were performed at the National Naval Medical Center, Bethesda, Maryland, on serum from 726 patients on whom standard tests for syphilis (S.T.S.) had given positive or doubtful results on two or more occasions and who had no clinical evidence or past history of syphilis. In all cases two separate specimens of serum were examined by the T.P.I. test. [It is not stated whether there was any disagreement between the results of tests on the two specimens.]

The T.P.I. test result was positive in 437 cases and negative in 289, an incidence of 39·8% non-specific S.T.S. reactions. The Kahn reaction had originally been found positive in 621 cases, and 248 (39·9%) were T.P.I.-negative. The Kolmer reaction was positive in 126 cases, but the T.P.I. reaction was negative in 27 (21·4%) of these. A test with cardiolipin antigen [nature not stated] had given 163 positive reactions, but serum from 48 of these patients gave a negative T.P.I. reaction.

A possible cause of non-specific S.T.S. reactions was present in only 60 of the 289 patients who were thought to have given such reactions in view of the negative T.P.I. result. These included cases of upper respiratory tract infection (18), malaria (9), infectious mononucleosis (6), pneumonia (6), virus pneumonia (4), and pregnancy (7 cases).

[These results emphasize the high proportion of cases in which no precipitating cause can be assigned for presumed non-specific S.T.S. reactions.]

A. E. Wilkinson

683. **Study of the TPI Test in Clinical Syphilis. III. Late Syphilis**

W. F. EDMUNDSON, S. OLANSKY, C. E. WOOD, and M. KAMP. *Archives of Dermatology* [*Arch. Derm. (Chicago)*] **71**, 387–390, March, 1955. 9 refs.

A comparative study of the reactivity of sera from 120 patients with late syphilis with the quantitative Kahn test, the quantitative Kolmer test using cardiolipin antigen, the V.D.R.L. slide test, and the treponemal immobilization (T.P.I.) test was carried out at the Venereal Disease Research Laboratory, Chamblee, Georgia. Both treated and untreated patients were included and the cerebrospinal fluid had been examined in all cases. Symptomatic neurosyphilis of various types was present in 57 cases, asymptomatic neurosyphilis in 44, cardiovascular syphilis in 15, and gummata in 4 (of the naso-oral cavity in 3, of the liver in one); 80 of the patients had been treated in the past.

The Kahn test gave a positive or doubtful (" reactive ") result in 64·9%, the Kolmer test in 85·4%, the V.D.R.L. test in 78·6%, and the T.P.I. test in 98·3% of the 120 patients. The only 2 patients in whom the T.P.I. reaction was negative were a man of 67 who had been adequately treated for early paresis in 1928 with arsphenamine and malaria, his serum having also given negative results in 1948, and a woman of 55 who had had a gumma of the palate which had been adequately treated with penicillin in 1951.

The authors consider that because of its high reactivity in late syphilis, the T.P.I. test may be helpful in the investigation of patients who have signs arousing suspicions of late syphilis which are not corroborated by the results of standard serum tests. This is especially likely to occur in patients with tabes and cardiovascular syphilis.

A. E. Wilkinson

684. **Experience with the New Pallida Antigen in Syphilitic Serology.** (Erfahrungen mit dem neuen Pallida-Antigen in der Lues-Serologie)

H. GROPPER. *Medizinische* [*Medizinische*] No. 10, 352–353, March 5, 1955. 5 refs.

The author surveys his experience at the Dermatological Clinic of the University of Tübingen in the use of the " pallida " reaction in 3,521 cases. Whereas the Wassermann reaction (W.R.) is dependent on the presence of a non-specific anti-lipid antibody, the pallida reaction is due to a specific antibody against spirochaetal protein. A positive reaction was obtained in 641 of the 3,521 cases, and the results are compared with those of the following tests simultaneously carried out: W.R. with cardiolipin antigen, W.R. with syphilitic liver, W.R. with beef heart, Kahn test, and Meinicke reactions (macroscopic and microscopic). With strongly positive sera the pallida reaction gave the highest number of positive results followed by the Meinicke reactions and Kahn test; the highest total number of positive results was given by the Meinicke reactions owing to their higher sensitivity with weakly positive sera. In one clinically diagnosed case of syphilis the pallida reaction was negative whereas the other reactions were positive; on the other hand the pallida reaction alone was positive in 3·1% of cases.

It was found that the sensitivity of these tests was in inverse proportion to their specificity; thus the original W.R. and the cardiolipin W.R., with relatively low sensitivity, gave more specific results than the more sensitive pallida and Meinicke reactions. False positive results with the pallida reaction may be due to lupus vulgaris. The pallida reaction tends to remain positive even in satisfactorily treated cases, unlike the cardiolipin W.R. and the original W.R., and it therefore cannot be used as a test of cure. In 2 recent cases of syphilis followed up with all the above tests the pallida reaction was the first

to become positive, followed closely by the two Meinicke reactions; owing to the early institution of treatment the ordinary W.R. never became positive in these cases.

It is noted that Nelson's treponemal immobilization test is superior to the pallida reaction in sensitivity and specificity. *F. Hillman*

685. **Pre-Columbian Osseous Syphilis. Skeletal Remains Found at Kinishba and Vandal Cave, Arizona, with Some Comments on Pertinent Literature**

H. N. Cole, J. C. Harkin, B. S. Kraus, and A. R. Moritz. *Archives of Dermatology* [*Arch. Derm. (Chicago)*] **71**, 231–238, Feb., 1955. 5 figs., 10 refs.

During an examination of 57 more or less complete skeletons found in Kinishba in the White Mountains and, in one instance, in Vandal Cave, Arizona, two examples of what the authors believed to be osseous syphilis were discovered. In one instance the appearances were those of diffuse gummatous osteoperiostitis of one tibia. In portions of the skull from the same skeleton there was evidence of periosteal thickening, but the changes were not considered to be pathognomonic of syphilis. The tibia of another skeleton showed what appeared to be the classic sabre-shin deformity of congenital syphilis. Examination of roof beams in the village, or pueblo, at Kinishba indicated that its 700 rooms were built in the 13th century. Evidence at Vandal Cave suggested that it was inhabited at a similar time and also earlier, probably in the 7th century. The authors consider these findings to indicate that syphilis was present in North America before the coming of Columbus. They discuss some evidence from the literature relating to the antiquity of syphilis in America, Europe, and Asia. *A. J. King*

686. **Treatment of Early Syphilis. Results with Penicillin G Procaine and Two Per Cent Aluminium Monostearate**

J. C. Cutler, S. Olansky, and E. V. Price. *Archives of Dermatology* [*Arch. Derm. (Chicago)*] **71**, 239–244, Feb., 1955. 1 fig., 5 refs.

Procaine benzylpenicillin in oil with 2% aluminium monostearate (PAM) has been used extensively in the treatment of syphilis, and in this paper results obtained at 5 treatment centres of the United States Public Health Service are reviewed, the observation period being 1 to 2 years. In the seronegative primary stage of the disease there was no obvious relationship between results and the dosage of PAM, as little as 300,000 units being effective. Of the patients in this group requiring further treatment, more than 60% were believed to have been reinfected, and the authors state that patients in the seronegative primary stage are particularly liable to reinfection because they have developed the least immunity. In the seropositive primary stage little advantage was gained by increasing the total dosage beyond 2,400,000 units, the reinfection rate being 12·7%; with a total dosage of 1,200,000 units 23% of patients required retreatment.

In the secondary stage the best results were obtained with the highest dosage used, namely, 9,600,000 units, the reinfection rate being 7%. In one centre where dosage was computed by body weight the most satisfactory results in the secondary stage of the disease (82% of cases) were obtained with the highest dosage, namely, 80,000 units per kg. body weight, but the results with 40,000 units per kg. were nearly as good (78%). With 20,000 units per kg. the percentage of successful results was 72, but with 10,000 per kg. there was an abrupt fall to 44. At another centre three schemes of treatment were employed: (1) 1,200,000 units in one injection; (2) two injections each of 1,200,000 units with 7 days' interval between the injections; and (3) 4 injections each of 1,200,000 units at intervals of 7 days; the percentages of successful results were 75·1, 83·1, and 91·6 respectively. At yet another centre the practice was to give a single injection of 2,400,000 units or two injections each of the same amount [with presumably 7 days' interval]. Treatment was successful in 94·6% and 91·8% of cases respectively, indicating that no advantage was to be gained by giving two injections of this amount. With 600,000 units twice a week for 8 weeks successful results were obtained in 93·8% of cases.

The only advantage of prolonging treatment beyond one or two injections appeared to be that the patient was in touch with the personnel of the treatment centre for a longer time, facilitating the tracing of contacts. This was important from the public health point of view, and a scheme of treatment was therefore devised in which an initial injection of 2,400,000 units of PAM was followed by two injections each of 1,200,000 units at intervals of 2 to 4 days. This ensured at least 3 visits to the clinic or, if the patient defaulted, the initial or " insurance " dose rendered the patient non-infectious and afforded an excellent chance of cure. *A. J. King*

687. **A Preliminary Report on the Effect of Carbomycin in Early Syphilis**

R. H. Buckinger, C. E. Hookings, and W. Garson. *Antibiotic Medicine* [*Antibiot. Med.*] **1**, 100–103, Feb., 1955. 2 figs., 1 ref.

A recent report (Turner and Schaeffer, *Amer. J. Syph.*, 1954, **38**, 81; *Abstracts of World Medicine*, 1954, **16**, 199) having shown that carbomycin, an antibiotic derived from *Streptomyces halstedii*, was " rather effective " at low serum levels in experimental syphilis in rabbits, a clinical trial of this antibiotic was undertaken at the Venereal Disease Clinic, Memphis, Tennessee.

A daily dose of 2 or 3 g. of carbomycin was given by mouth to 11 patients with dark-field positive primary or secondary syphilis. *Treponema pallidum* disappeared from the lesions in 36 to 72 hours after the initial dose. Side-effects, which were slight, were observed in only 2 cases.

[This is a preliminary report of a rather inconclusive clinical trial, but it indicates that carbomycin has some effect on *T. pallidum* and that in the dosage employed it is relatively free from side-effects. Longer observation of the patients and laboratory tests to determine the blood level of the antibiotic and serological results of treatment will be necessary before the value of carbomycin in the treatment of syphilis can be assessed.] *Robert Lees*

Tropical Medicine

688. **Long Term Treatment of Leprosy with Cortisone**
E. C. DEL POZO, A. GONZÁLEZ-OCHOA, S. RICO VENEGAS, M. MARTÍNEZ-BAEZ, and M. ALCARAZ. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **24**, 51–56, Jan., 1955. 2 refs.

The results of long-term administration of cortisone to 9 lepers with continuous or frequently recurring manifestations of the acute reaction which made treatment with diaminodiphenylsulphone (DDS) impossible are reported from Mexico. Cortisone was given by mouth in a daily dosage of 25 to 175 mg., depending on the amount necessary to suppress the reaction, for as long as 12 months in 4 of the cases, in all of which the manifestations of the reaction—erythema nodosum and erythema multiforme—were suppressed. Some general improvement was observed in all cases and there was no evidence of dissemination of the infection. Moreover, DDS could be given with safety in those cases in which it had previously provoked a reaction; in 2 cases DDS was given for 6 months after cessation of cortisone therapy without producing a reaction. Administration of cortisone had to be discontinued because of psychosis in one case (this patient had a history of mental disease), renal complications in one, and lack of cooperation in 5 cases. No toxic effects were noted. Two of the cases in which there was a rapid response to cortisone are described in detail. The authors state that the beneficial effects of cortisone in this complication of leprosy exceeded their expectations. *William Hughes*

689. ***iso*Nicotinic Hydrazide in the Treatment of Leprosy**
J. H. HALE, B. D. MOLESWORTH, D. A. RUSSELL, and L. H. LEE. *International Journal of Leprosy* [*Int. J. Leprosy*] **22**, 297–302, July–Sept., 1954. 8 figs., 12 refs.

A clinical trial of isoniazid in the treatment of 100 patients with leprosy, mostly the lepromatous or atypical form of the disease, was undertaken at the Sungei Buloh Settlement, Selangor, Malaya. The initial dosage was 25 mg. daily, increased gradually to 100 or 150 mg. daily, the latter being the maximum dose tolerated. Biopsy specimens from skin lesions were examined before treatment and again after 6 months. Treatment was stopped after 8 months because the progress of the 83 patients who received the drug for this length of time was obviously inferior to that of patients being treated with sulphones.

In the first few weeks the patients gained weight and enjoyed a general feeling of well-being. At the end of 8 months the results were as follows. Of 5 patients with the tuberculoid form of the disease, one improved and 4 showed no improvement; of 38 atypical cases the condition was improved in 18, stationary in 12, and worse in 8; of 40 lepromatous cases the condition was improved in 7, stationary in 21, and worse in 12. On the whole the drug was well tolerated in a dosage up to 100 mg. daily. In most cases there was a short period of nausea and giddiness, and in a few cases gastritis occurred, this being severe in one case. Oedema of the hands and feet was noted in 2 patients and jaundice in one. In many of the lepromatous and atypical cases erythema nodosum developed. An unusual reaction, which the authors had not previously observed, occurred in 3 tuberculoid cases, the lesions becoming intensely congested and dark, and in one case ulcerating.

It is concluded that isoniazid has some therapeutic value in leprosy and that it probably kills many of the bacilli. It is, however, much inferior to diaminodiphenylsulphone, and is not therefore recommended as the sole therapeutic agent in the treatment of leprosy. *F. Hawking*

690. **Lepromin and Tuberculin Tests in Venezuelan Leprosy Foci. Induction of Lepromin Reactivity by BCG Vaccination**
J. CONVIT and E. RASSI. *International Journal of Leprosy* [*Int. J. Leprosy*] **22**, 303–310, July–Sept., 1954. 2 figs., 1 ref.

The lepromin and tuberculin reactions before and after administration of B.C.G. vaccine were studied in 8,353 inhabitants of rural areas of Venezuela, where leprosy is endemic. Of this number, 83·8% gave a positive reaction to the Mitsuda test, the percentage of positive reactions increasing with age from 58 in the group 0 to 4 years to 94 in the group 25 to 44 years. The reaction to the Mantoux test was positive in 37·5% of cases; with this test also the percentage of positive results rose with age from 5·6 in the group 0 to 4 years to 60 in the group 25 to 44 years. The coefficient of correlation between the reactions to the two tests was comparatively low (0·44). Of the subjects giving a positive reaction to the lepromin test, 45% were also tuberculin positive; of those giving a negative reaction to the lepromin test, only 3% were tuberculin positive. Altogether 960 lepromin-negative subjects were vaccinated with B.C.G. and 92·2% of these became lepromin-positive. It is considered that B.C.G. vaccination will prove an effective prophylactic measure against leprosy, at least in rural areas. *F. Hawking*

691. **A Report on Intestinal Disorders Accompanied by Large Numbers of *Dientamoeba fragilis***
M. YOELI. *Journal of Tropical Medicine and Hygiene* [*J. trop. Med. Hyg.*] **58**, 38–41, Feb., 1955. 2 refs.

In this paper from the Hebrew University–Hadassah Medical School, Jerusalem, 9 cases are described of intestinal disorder characterized by explosive diarrhoea, severe abdominal pain, cramps, nausea, and mild fever and the finding of large numbers of *Dientamoeba fragilis* in the stools. No other pathogenic organism could be detected on microscopical examination or culture. *Blastocystis hominis* was prevalent in most of the stool specimens.

It is considered that the presence of *D. fragilis* was due to change in the intestinal environment and not to pathogenicity of the amoeba. Three of the patients had previously suffered from dysenteric infection. Oxytetracycline by mouth in a dosage of 2 g. daily for 6 or 7 days with a high-protein diet and added vitamins resulted in rapid cure. There was no relapse over a period of 5 months. The author suggests that the antibiotic was effective by changing the intestinal flora and not by any direct amoebicidal action. *W. H. Horner Andrews*

692. **Pentaquine and Quinine in the Treatment of Korean Vivax Malaria. A Controlled Study in 101 Patients**
W. H. HALL and E. M. LATTS. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **45**, 573–579, April, 1955. 24 refs.

693. **Oxygen Therapy of Ascariasis in Patients Suffering from Dysentery.** (Оксигенотерапия аскаридоза у больных дизентерией)
I. F. JUPANENKO. *Советская Медицина* [*Sovetsk. Med.*] 68–70, No. 3, March, 1955.

It has been known for some time that in the presence of ascariasis the course of acute bacillary dysentery is often protracted and may become chronic. In such cases a cure can be achieved only after the expulsion of the intestinal parasites. A recent study of acute dysentery showed that whereas in patients infested with *Ascaris* appropriate treatment of the dysentery arrested the diarrhoea in an average of 9·7 days, in patients without ascariasis a similar result was obtained in an average of 7·3 days. Moreover, while ascariasis was present in 16% of patients suffering from chronic dysentery, only 4·7% of all patients suffering from dysentery were infested.

The use of orthodox anthelminthics is contraindicated in acute dysentery, but oxygen therapy has proved harmless and most effective. Oxygen is introduced into the stomach intermittently to a total volume of 1,500 to 2,000 ml. within about 10 to 12 minutes by means of a thin rubber tube. More rapid introduction of the oxygen gives rise to eructation and epigastric pain. The oxygen quickly passes into the intestines, but causes no discomfort or symptoms of any kind. After 24 hours the procedure is repeated. No laxative is given, but 2 to 5 days later dead parasites are passed with the stools in 80% of cases treated. Oxygen therapy should be initiated only after the symptoms of the acute infection have moderated, and it is contraindicated in the presence of symptoms of pericolitis. *A. Orley*

694. **Hepatic Schistosomiasis in Children**
A. EL-GHOLMY, M. NABAWY, M. GABR, S. AIDAROS, and A. OMAR. *Journal of Tropical Medicine and Hygiene* [*J. trop. Med. Hyg.*] **58**, 25–33, Feb., 1955. 8 figs., 11 refs.

The clinical and laboratory findings in 127 cases of hepatic schistosomiasis in childhood are reported from Kasr-el-Aini Faculty of Medicine, Cairo. The ages of the patients (100 males and 27 females) ranged from 5 to 16 years. All the patients had urinary infection and 19 had intestinal infection as well, as indicated by the presence in the stools of *Schistosoma haematobium* (11 cases) and *S. mansoni* (8 cases). Liver biopsy was performed in 33 cases, including 12 with intestinal infection. No hepatic changes were noted in 7 of the cases of urinary infection only; in the remaining 26 cases the liver changes indicated four stages in the disease process: (1) pre-cirrhosis; (2) early cirrhosis, with fibroblastic proliferation and cellular infiltration; (3) established cirrhosis, with definite fibrosis; and (4) advanced cirrhosis. There was no correlation between clinical evidence of enlargement of the liver and spleen and the liver biopsy findings. Advanced cirrhosis was not observed in patients who had had schistosomiasis for less than one year. In 3 cases in which splenectomy was performed the pressure in the portal vein was found to vary from 280 to 330 mm. saline. From the results of splenic venography in 10 other cases the authors consider that portal hypertension frequently occurs in this disease. A marked diminution in the size of the liver and spleen followed treatment in the pre-cirrhotic and early stages, but not in the established and advanced stages.

[This article contains useful material, but the pathological details are not well described. The selection of cases for liver biopsy is said to be random, yet they comprised 12 of the 19 cases of urinary infection with intestinal involvement and 21 of the 108 cases of urinary involvement only. The analysis of results consequently suffers somewhat.] *W. H. Horner Andrews*

695. **Peculiarities of Phosphorus Metabolism in Malnutrition and Kwashiorkor.** (Les particularités du métabolisme du phosphore dans la malnutrition et le kwashiorkor)
K. HOLEMANS, A. LAMBRECHTS, and H. MARTIN. *Presse médicale* [*Presse méd.*] **63**, 154–155, Feb. 5, 1955. 1 fig., 14 refs.

Having formed the opinion that the diet of children suffering from kwashiorkor is lacking in mineral elements, most probably phosphorus and calcium, as well as in protein, the authors, working at Feshi, Belgian Congo, and the University of Liège, carried out a series of balance experiments which proved the theory to be correct. They found that children suffering from kwashiorkor and living on a diet providing only 30 mg. of phosphorus per kg. per day absorbed 56% and retained 35% of the dietary phosphorus (compared with 69% and 15% respectively reported by Macy for healthy children in the U.S.A. on similar diets). When the intake of phosphorus was increased to 124 mg. per kg. of diet per day the absorption and retention values rose to 67% and 59% respectively. They further showed that the average ratio of faecal to urinary excretion of phosphorus, which is normally between 0·43 and 0·70, in 28 children with kwashiorkor was 4·7, and that treatment with 20,000 i.u. of vitamin D daily in 3 cases made the ratio still more abnormal. The albumin:globulin ratio in the serum was also shown to be inversely related to the ratio of faecal:urinary phosphorus excretion, and the phospholipid content of the faeces was found to be increased about 14-fold in patients with kwashiorkor. *H. E. Magee*

Nutrition and Metabolism

696. **Studies of the Absorption and Metabolism of Glucose following Injury. The Systemic Response to Injury**
J. M. HOWARD. *Annals of Surgery* [*Ann. Surg.*] **141**, 321–326, March, 1955. 6 figs., 12 refs.

Glucose tolerance tests were performed on 14 casualties with various degrees of injury, all aged 18 to 30 years, who had been on "combat duty" in Korea for 10 to 40 days previously, and on 6 healthy soldiers who had not been in action. Tests on the casualties were performed during the week following injury and repeated once or more when feasible, 100 g. of glucose being given by mouth after a 12-hour fast. In addition, insulin tolerance tests were performed on 3 healthy soldiers, 4 casualties with minor injuries, and 6 casualties with severe injuries, 0·1 unit of crystalline insulin per kg. body weight being given intravenously and the blood glucose level determined at intervals for 2 hours.

The glucose tolerance of the healthy soldiers was normal, fasting blood sugar concentration of 78 to 90 mg. per 100 ml. rising to a mean peak level of 134 mg. per 100 ml. in 30 minutes and returning to fasting level within 3 hours. In 4 men with minor injuries the fasting concentration averaged 95 mg. per 100 ml. and rose to an average peak of 165 mg. per 100 ml. in 45 minutes. In 10 soldiers with major injuries on whom 14 glucose tolerance tests were performed during the first week the average blood sugar concentration was initially 110 mg. per 100 ml., rising to an average peak of 202 mg. per 100 ml. at 60 minutes, and being still above fasting level after 4 hours. Insulin tolerance tests demonstrated a similar correlation between the degree of resistance to insulin and the degree of injury. Both types of abnormality tended to diminish with recovery. The physiological implications of these findings and their possible explanation are discussed. *Norval Taylor*

697. **Comparison of the Volume of Distribution of Sucrose, Inulin and Thiosulfate in Human Subjects**
D. IKKOS. *Metabolism* [*Metabolism*] **4**, 1[illegible]–28, Jan., 1955. 1 fig., 15 refs.

The volumes of distribution of injected sucrose, inulin, and thiosulphate were compared at the Serafimerlasarett, Stockholm, in 12 healthy subjects, in 15 patients with endocrine disorders (mostly acromegaly), in one with idiopathic hypokalaemia, and in one with rheumatoid arthritis who had been receiving treatment with deoxycortone acetate.

The volume of distribution of sucrose (V_s) was measured simultaneously with that of thiosulphate (V_{th}) or inulin (V_{in}). It was found that with a constant rate of infusion V_s increased with the duration of the infusion, and for purposes of comparison the author took the value obtained after 150 minutes. V_{in} was found to be smaller than V_{th}, the ratio $V_{in} : V_{th}$ being $0{\cdot}95 \pm 0{\cdot}02$ for the control subjects and $0{\cdot}94 \pm 0{\cdot}07$ for the patients. On the other hand V_s was greater than V_{th}, the ratio $V_s : V_{th}$ being $1{\cdot}34 \pm 0{\cdot}05$ for the controls and $1{\cdot}33 \pm 0{\cdot}06$ for the patients. In 16 subjects both of these comparisons were made and, using V_{th} as the point of reference, the calculated ratio $V_s : V_{in}$ was $1{\cdot}46 \pm 0{\cdot}06$. The author considers that the close similarity between the volumes of distribution of inulin and thiosulphate provides some evidence that they are distributed in the same compartment of the body fluid.

G. A. Smart

698. **Primary Vitamin D Refractory Rickets. II. Metabolic Studies during Treatment with Massive Doses of Vitamin D.** [In English]
R. ZETTERSTRÖM and J. WINBERG. *Acta paediatrica* [*Acta paediat. (Uppsala)*] **44**, 45–61, Jan., 1955. 7 figs., 28 refs.

The aetiology of vitamin-D-resistant rickets is still obscure in that it is not known why such large doses of the vitamin are necessary in treatment. Some workers have suggested that the cause is either an intrinsic resistance to vitamin D or a metabolic deficiency secondary to the high urinary excretion of phosphates. Others have pointed out that metabolic studies are difficult to interpret because the changes are the result not only of the direct action of the vitamin but also of altered parathyroid function.

The present authors in this paper from Karolinska Sjukhuset, Stockholm, describe the results of a study of the metabolism of 2 children with primary vitamin-D-refractory rickets. During a control period there was hypophosphataemia with excessive urinary loss in spite of a normal absorption of phosphate. However, the ability to conserve phosphate remained when absorption was reduced, so that the defect could not be due entirely to urinary loss. Serum calcium values were low or normal, and both absorption and excretion were reduced. When treatment with vitamin D began there was an immediate fall in the serum levels of phosphate and calcium, though urinary excretion of phosphate remained unchanged. Later there was a rise in the serum phosphate level, again with little change in urinary excretion. This suggested that tubular reabsorption of phosphate increased, if it was assumed that glomerular filtration rate remained unchanged. The serum calcium level also rose. These changes occurred in spite of retention of calcium and phosphate, as shown by balance studies, so that absorption must have increased. It thus appeared that vitamin D acted on the gut, on the kidneys, and on bone, but whether this was a direct action or a secondary effect is not clear. A practical point that arises from this study is that a fall in the serum alkaline-phosphatase level is the best guide to remineralization of bones in this condition. *A. Paton*

Gastroenterology

699. **Esophageal Reflux in Simple Heartburn**
C. A. FLOOD, J. WELLS, and D. BAKER. *Gastroenterology* [*Gastroenterology*] **28**, 28–33, Jan., 1955. 13 refs.

In an investigation carried out at the Presbyterian Hospital (Columbia University), New York, into the occurrence of oesophageal reflux as a cause of heartburn, 33 patients complaining of heartburn as a major symptom, but without hiatus hernia, were studied. In each case an injection of histamine was given, a stomach tube was passed until the tip lay in the oesophagus 30 cm. from the incisor teeth, and with the patient lying on the right side and the head of the table lowered periodic aspiration was carried out for 10 minutes. The tube was then advanced successively to the 35-cm. and 40-cm. marks, aspiration being continued for 10 minutes at each level. The tube was finally passed into the stomach and the gastric contents aspirated. Free acid was present in 12 cases in the fluid aspirated at the level of 30 cm. and in 5 others at 35 cm. All but one of the patients had free acid in the gastric juice. Oesophagoscopy was performed on 5 patients, 2 of whom were found to have oesophagitis with superficial ulceration just above the cardia, while the lower oesophagus was mildly reddened in 2 other cases and normal in the remaining case. Ten patients were subjected to a long and careful fluoroscopic examination, but reflux of barium could be shown to occur in only 2 of them.

The discrepancy between the results of intubation and of radiology might suggest that the presence of a tube in the oesophagus tends to induce regurgitation from the stomach, and it was noted that in almost all these cases gagging occurred, particularly on introduction of the tube and on advancing its position. In a similar investigation of 52 patients with gastro-intestinal disease but without frequent heartburn, however, gagging was just as frequent, but acid was not found in a single case at the 30-cm. level and in only 2 cases at 35 cm. The authors suggest that changes in the tone and activity of the smooth muscle in the region of the cardia in patients with heartburn may account for this difference, together with various other factors which may affect the competence of the sphincter mechanism at the lower end of the oesophagus. Donnelly (*Brit. J. Radiol.*, 1953, **26**, 441; *Abstracts of World Medicine*, 1954, **15**, 218) suggested that frequent belching might lead ultimately to the development of a hiatus hernia. Since belching is a common symptom in patients with heartburn, it is possible that incompetence at the cardia also results from the repeated mechanical stress so caused.

Denys Jennings

700. **Acute Caustic Soda Injuries of the Oesophagus**
P. MARCHAND. *South African Medical Journal* [*S. Afr. med. J.*] **29**, 195–205, Feb. 26, 1955. 10 figs., 20 refs.

STOMACH AND DUODENUM

701. **The Special Significance of Concomitant Gastric and Duodenal Ulcers**
H. DAINTREE JOHNSON. *Lancet* [*Lancet*] **1**, 266–270, Feb. 5, 1955. 3 figs., 8 refs.

The author contends that gastric hypomotility and retention are the main factors in the aetiology of gastric ulcer, and that although duodenal ulceration is usually associated with gastric hypersecretion and rapid emptying, it may, by producing pyloric stenosis, none the less predispose to the development of a concomitant or subsequent gastric ulcer. The incidence of concomitant gastric and duodenal ulcers among cases of peptic ulceration is usually regarded as about 5%. Of the author's own series of 311 patients operated upon for peptic ulcer, 29 (9%) had lesions of both organs. An analysis of these 29 cases with 90 others treated by colleagues showed that in 34 cases (29%) both ulcers were present when the patient was first investigated or were found together at operation after radiology had failed to detect either. Of the remaining 85 cases, in 79 (66%) there was evidence that the duodenal ulcer had developed first, and only in 6 cases (5%) did the gastric ulcer precede the duodenal. It is therefore suggested that in the majority of cases of double ulceration the duodenal ulcer appears first, and that the gastric ulcer develops as a direct consequence of the effect of the former on gastric emptying.

The suggestions that reflux oesophagitis may sometimes cause hiatus hernia and that gastric ulcer may be a late complication of vagotomy are also made [but are not really substantiated].

[Since a scar, with or without stenosis, was the only operative finding in the duodenum in 78 out of 110 cases analysed, the use of the term "concomitant" is unjustified in the abstracter's opinion.]

Guy Blackburn

702. **Social Aspects of Peptic Ulcer**
F. AVERY JONES. *Journal of the Royal Institute of Public Health and Hygiene* [*J. roy. Inst. publ. Hlth*] **18**, 64–74, March, 1955. 2 figs., 20 refs.

In this paper the environmental factors which may influence the occurrence of peptic ulceration are reviewed with particular reference to the prevalence of the condition and its social, occupational, and geographical distribution. In a survey carried out in 1951 on a sample of over 6,000 persons drawn from various occupational groups working in or near London 5·8% of the men and 1·9% of the women aged 15 to 64 years had a history of peptic ulceration. In both sexes the incidence increased with age to a maximum at 45 to 54 years and thereafter declined. Studies in various Euro-

pean countries have shown that during the last 50 years acute ulceration among women in the younger age groups has been becoming relatively less common, while an increase has occurred in chronic ulceration among men. This increase among men has been due largely to increased incidence of duodenal ulceration and it is less certain whether gastric ulceration has also contributed to the increase. The difficulty of interpreting the available mortality data on this subject is discussed.

The author's personal impression that the ratio of duodenal to gastric ulcers among patients admitted to the Central Middlesex Hospital, London, with perforation has increased during the past 15 years has been confirmed by data from over 30 other hospitals. The relative increase in this ratio between 1938 and 1948 was not materially different as between hospitals in rural and urban areas. However, in each year the well-known difference between urban and rural areas in respect of the ratio was well demonstrated. The relative incidence of gastric and duodenal ulcer also varies in different countries, and in different regions of the same country. In part such geographical differences could be explained as being due to differences in the degree of urbanization of the areas compared. However, the incidence of gastric ulcer, but not of duodenal ulcer, has been shown to be associated with social class, so that differences in the standard of living may also play a part.

In the 1951 London survey the incidence of peptic ulceration was shown to be abnormally high among doctors and also among unskilled workers. However, this apparent association may be artificial, the standard of diagnosis being higher among doctors, and men with peptic ulcer tending to seek the sheltered employment of unskilled work. Among business executives, persons holding responsible positions in industry, and foremen there was also an unusually high incidence of ulceration, which was largely duodenal.

The author expresses the belief that the aetiological factors responsible for gastric and duodenal ulcer will ultimately be found to differ, and to be related to environmental factors which may well be associated with modern feeding habits or methods of processing food.

E. A. Cheeseman

703. **Treatment of Haemorrhage from Peptic Ulcer by Continuous Intragastric Milk Drip**

D. W. Ashby and D. Whitehouse. *British Medical Journal* [*Brit. med. J.*] **1**, 512–515, Feb. 26, 1955. 2 figs., 21 refs.

A regimen for the treatment of cases of haemorrhage from peptic ulcer which has been used since 1950 in all cases admitted to one of the hospitals in the Gateshead Group is described. It provides for a continuous intragastric milk drip at a rate of 5 to 6 pints (2·8 to 3·4 litres) in 24 hours and a generous bland diet at 4-hourly intervals, the total intake being about 3,700 Calories a day. In a very few instances aluminium hydroxide gel was also given, and all patients received adequate blood transfusions. In assessing the results the authors do not exclude deaths from related conditions or the late complications of surgery. Of 100 patients treated, 7 died, 2 from haemorrhage, 3 from late complications of surgery, and 2 from other associated conditions.

The authors believe that in patients given this regimen haemorrhage ceases earlier than in patients given conventional treatment, but that the incidence of recurrent haemorrhage is probably not reduced.

G. A. Smart

704. **Treatment of Chronic Hyperchlorhydric Gastritis with Histidine.** (Лечение гистидином больных хроническими гастритами с повышенной кислотностью)

A. E. Sigal. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **33**, 78–81, Feb., 1955. 3 refs.

The effect of treatment with histidine in 94 cases of hyperchlorhydric gastritis and 53 of peptic ulcer (21 gastric and 32 duodenal) is described. From 25 to 30 intramuscular injections of 5 ml. of 4% histidine was the standard course; in 24 cases a second course was given 3 months later owing to a recurrence of symptoms.

The results were impressive; the symptoms diminished noticeably after the first 10 injections, and had disappeared in almost all cases by the end of the first course. The total acidity and free acid content of the gastric juice were reduced by 10 to 25 units, and in the cases of ulcer the crater was no longer evident on radiological examination. In 2 cases of gastritis and one of peptic ulcer side-effects developed after the first or second injection in the form of faintness, pallor, sweating, and pain in the substernal region lasting about 15 minutes; these symptoms recurred when further injections were given, and the treatment had to be discontinued in all 3 cases.

[Histidine treatment was much in favour in Great Britain some years ago until the unqualified condemnation of leading authorities consigned it to oblivion. Nonetheless, in the abstracter's experience it did appear to be effective in accelerating the healing of peptic ulcers, though one very obstinate and long-standing case required no less than 75 injections.]

L. Firman-Edwards

705. **Hypertrophic Gastritis. Report of Two Cases and Analysis of Fifty Pathologically Verified Cases from the Literature**

S. S. Fieber. *Gastroenterology* [*Gastroenterology*] **28**, 39–69, Jan., 1955. 10 figs., bibliography.

The author describes in detail 2 recent cases of hypertrophic gastritis and reviews 50 proved cases from the literature. His conclusions from the literature may be summarized as follows. The disease is rare. The common symptoms in order of frequency are pain, loss of weight, vomiting, and haemorrhage. In some cases there is a tendency to hypoacidity and in some hypoalbuminaemia is observed. In diagnosis *x*-ray examination is more useful than gastroscopy, but the histological appearances of biopsy specimens are helpful. The perplexing pathological features are discussed, some of those encountered being increased mucosal rugae, increased cellular infiltration and oedema, and, rarely, glandular hyperplasia. The stomach is thickened and very heavy. Clinical diagnosis, particularly the differential diagnosis from various forms of neoplasia of

the stomach, is difficult. Symptoms are intractable and various forms of conservative treatment have been tried with little success. In cases of recurrent haemorrhage, intractable pain, obstruction, or suspected malignant disease subtotal gastrectomy is advised.

Partial gastrectomy was performed with success in the author's 2 cases. In one the resected portion of the stomach weighed 750 g., four times the weight of the average gastrectomy specimen. The follow-up period in these 2 cases and those from the literature in which operation was performed is as yet too short for any conclusions to be drawn. *J. Naish*

706. **Massive Gastrointestinal Hemorrhage due to Familial-hereditary Telangiectases**
L. L. HARDT, F. STEIGMANN, S. A. LEVINSON, and I. GORE. *Gastroenterology* [*Gastroenterology*] **28**, 70–79, Jan., 1955. 4 figs., 22 refs.

The authors describe 6 cases of hereditary haemorrhagic telangiectasia causing severe gastro-intestinal bleeding seen during the past few years. In 3 cases no telangiectasia was visible on clinical or gastroscopic examination, but the diagnosis was confirmed at necropsy in 2 of the cases and by proctoscopic examination in one case. In the other 3 cases the diagnosis was based on the presence of facial, oral, pharyngeal, and rectal telangiectasia with a suggestive family history of epistaxis and other forms of haemorrhage. At necropsy in one case the telangiectases were seen to be confined to the small intestine.

The authors' object in presenting these 6 varied cases is to emphasize the difficult diagnosis of this condition. They suggest that the disease should be suspected in any case of repeated gastro-intestinal haemorrhage with negative radiological findings, even in the absence of a family history and visible telangiectasia. They recommend proctoscopy and gastroscopy as useful diagnostic aids. *J. Naish*

707. **Uropepsin Excretion in Gastroduodenal Disease. A Correlative Clinical Study**
D. A. CUBBERLEY, A. E. DAGRADI, H. O. CARNE, and S. J. STEMPIEN. *Gastroenterology* [*Gastroenterology*] **28**, 80–87, Jan., 1955. 14 refs.

The value of estimating uropepsin excretion in the diagnosis of gastroenterological disorders and in the study of adrenocortical activity was investigated at the Veterans Administration Hospital, Long Beach, California. In 81 patients with gastritis the findings at gastroscopy were correlated with the values for excretion of uropepsin. It was found that the output of uropepsin tended to be low in atrophic gastritis and high in hypertrophic gastritis. However, when anticholinergic drugs were given to patients with hypertrophic gastritis the output was normal. In atrophic gastritis there was a close parallel between the low uropepsin excretion and gastric acid secretion as measured by histamine stimulation. It was also found that a normal appearance of the gastric mucosa was not necessarily associated with an output of uropepsin within the normal range. In 21 patients with duodenal ulcer who were receiving " banthine " (methantheline) or atropine the level of uropepsin excretion was in the " low normal " range, whereas in 8 patients not receiving anticholinergic drugs the output was above normal and was reduced on administration of atropine.

Uropepsin excretion was usually diminished in cases of gastric carcinoma and of partial gastrectomy, normal in cases of benign gastric ulceration and of gastroenterostomy alone, and increased after administration of corticotrophin. The authors state that uropepsin level should not be used as an index of adrenocortical activity unless the morphological state of the gastric mucosa is known. *P. I. Reed*

708. **Levels of Intragastric and Intraduodenal Acidity**
M. ATKINSON and K. S. HENLEY. *Clinical Science* [*Clin. Sci.*] **14**, 1–14, Feb., 1955. 5 figs., 17 refs.

An investigation was undertaken at the Postgraduate Medical School of London to determine the acidity of the contents of the stomach and of the duodenum in healthy subjects and patients with peptic ulcer. A double-lumen tube was used to obtain simultaneously samples of the contents of the stomach and of the first part of the duodenum. The patients retained the tube, were not confined to bed, and ate a standard diet. The position of the tube was checked radiologically at intervals of 3 to 4 hours, and 4-ml. samples of the contents of the stomach and of the first part of the duodenum were taken each hour for periods of 12 to 24 hours.

The mean level of the acidity of the gastric contents was higher in the duodenal-ulcer group and lower in the gastric-ulcer group than in the controls. In all three groups there was a fall in acidity during the night, this being least marked in the duodenal-ulcer group and most prominent in the gastric-ulcer group. The mean level of the acidity of the duodenal contents increased during the day in the patients with duodenal ulcer, falling to normal at night, whereas in the patients with gastric ulcer it was reduced during the day; there was no fall at night in the controls. The post-prandial changes in the acidity of the gastric contents were reflected in the duodenal contents.

It appears that the fluid bathing a duodenal ulcer is more acid than that bathing a gastric ulcer.
Joseph Parness

709. **Biopsy Studies of the Gastric Mucosa**
R. S. YLVISAKER, J. B. CAREY, J. MYHRE, and J. B. CAREY, jun. *Gastroenterology* [*Gastroenterology*] **28**, 88–102, Jan., 1955. 10 figs., 24 refs.

A year's experience at the University of Minnesota Hospitals, Minneapolis, of the use of Benedict's operating gastroscope is reviewed and the appearances of the gastric mucosa in 77 examinations carried out without complications on 75 patients are compared with the histological findings at biopsy. The specimens obtained were classified histologically as: (1) normal mucosa; (2) superficial gastritis; and (3) atrophic gastritis. Hypertrophic gastritis was diagnosed gastroscopically in 13 out of 36 cases with a histologically normal mucosa. The authors consider that this finding should be " considered a variation probably related chiefly to the func-

tional state of the muscularis mucosae". Otherwise in the normal mucosa there was excellent correlation between the gastroscopical and histological findings. This was not so, however, in cases of atrophic gastritis, an appreciable proportion of histologically proved cases being missed at gastroscopy. This investigation confirmed the findings of others—namely, that atrophic gastritis is common in patients with gastric ulcer but unusual in those with duodenal ulcer; that it is usually associated with achlorhydria; and that the incidence of atrophic gastritis increases with age, some 90% of the patients being over 50 years of age.

There was only one case of carcinoma in the series, and this was actually missed at biopsy. In one case of proved pernicious anaemia and one of subacute combined degeneration of the spinal cord with a normal blood picture atrophic gastritis was found at biopsy. Discussing symptoms in patients without ulcer, gall-bladder disease, or cancer the authors state that apart from a higher incidence of pain after eating and flatulence in patients with gastritis than in those with a normal mucosa no symptom complex specific for gastritis was noted.

P. I. Reed

LIVER AND GALL-BLADDER

710. **Comparison of Esophagoscopic and Roentgenologic Diagnosis of Esophageal Varices in Cirrhosis of the Liver**

I. B. BRICK and E. D. PALMER. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **73**, 387–389, March, 1955. 5 refs.

A study of 172 cases of proved cirrhosis of the liver is presented. Relative diagnostic merit of esophagoscopic and roentgen diagnosis of esophageal varices is compared. In this series, varices were present in 62·7% of the cases by esophagoscopy and in 14% by roentgen ray. —[Authors' summary.]

711. **Ammonium Tolerance in Liver Disease: Observations Based on Catheterization of the Hepatic Veins**

L. P. WHITE, E. A. PHEAR, W. H. J. SUMMERSKILL, and S. SHERLOCK. *Journal of Clinical Investigation* [*J. clin. Invest.*] **34**, 158–168, Feb., 1955. 6 figs., 24 refs.

At the Postgraduate Medical School of London the ammonium content of peripheral venous blood and blood obtained by catheterization from the hepatic and, in some cases, the renal veins was estimated by the Conway technique in 11 healthy subjects, 6 patients with virus hepatitis, 26 with hepatic cirrhosis, and 8 with miscellaneous conditions (including 3 cases of carcinoma involving the liver or bile ducts) before and 30, 60, and 120 minutes after giving a dose of 3 g. of ammonium chloride by mouth. In the control subjects the mean ammonium concentration in peripheral venous blood was initially slightly above that in hepatic venous blood. After the ingestion of ammonium chloride the former rose moderately to a peak at 30 minutes and then rapidly declined, while the latter rose more slowly and reached its peak only after 60 minutes. Both returned to the initial levels within 120 minutes. In patients with acute hepatitis or cirrhosis with poor liver function both the initial ammonium content and its rise after ingestion of the salt were greater in hepatic venous than in peripheral venous blood, whereas in patients with cirrhosis and evidence of collateral circulation the rise of ammonium level was greater in peripheral venous than in hepatic venous blood. The initial levels in all the patients with liver disease were higher than those found in the control subjects.

The rise in hepatic venous ammonium content after a loading dose of ammonium chloride by mouth is a sensitive test of hepatocellular function, since in the presence of liver-cell damage the liver is unable to remove the ammonium reaching it from the gastro-intestinal tract, which seems to be the main source of ammonium in the blood. In patients with cirrhosis and portal hypertension but with good liver function, however, some portal venous blood is diverted into the systemic circulation through collateral vessels, so that the ammonium level in the peripheral blood is elevated to a greater extent than that in the hepatic venous blood.

P. C. Reynell

712. **Hepatic Function following Wounding and Resuscitation with Plasma Expanders**

R. SCOTT and J. M. HOWARD. *Annals of Surgery* [*Ann. Surg.*] **141**, 357–365, March, 1955. 5 figs., 8 refs.

From this study, no evidence was obtained that dextran or modified gelatine was deleterious to hepatic function. Following resuscitation with the plasma expanders, the alteration in the panel of hepatic function studies was less marked than when the casualties were resuscitated with stored, citrated blood. This observation does not lead to the conclusion that a plasma expander is superior to whole blood. The most likely implication would be that the casualty resuscitated with plasma expander does not receive pigment containing compounds that produce alterations in the standard hepatic function tests which simulate hepatic insufficiency.—[Authors' summary.]

713. **Anatomico-clinical Correlation of Post-hepatitis Liver Biopsies**

R. ARMAS-CRUZ, O. PERALTA, G. LOBO-PARGA, M. DAVILA, R. DEL RIO, and M. OSSANDON. *Gastroenterology* [*Gastroenterology*] **27**, 811–828, Dec., 1954. 9 figs., 27 refs.

Liver biopsy was performed at the Hospital del Salvador, Santiago, Chile, on 25 patients recovering from virus hepatitis. The Silverman needle was used and the intercostal approach chosen. The examination was carried out either during the convalescent period immediately after the acute attack or at an interval of 5 months to 5 years after the initial attack, 5 patients undergoing biopsy on 2 occasions.

The histological changes commonly seen consisted in occasional fatty infiltration of the liver cells, inclusion granules of haemosiderin, and biliary thrombi. The most frequent change, however, was an increase in the fibrous tissue of the portal spaces. Collagenization of the argentophil reticulum was also sometimes en-

countered. In all 9 cases in which biopsy was performed during the immediate convalescent period "moderate" changes were seen, always involving the portal spaces. Of the 21 specimens obtained at a later stage, 6 showed "moderate" changes and 2 "marked" changes, the latter in one case being characteristic of chronic hepatitis and in the other of multiple nodular hyperplasia.

The authors stress the value of liver biopsy as an objective method of determining the presence or absence of residual liver damage in cases in which there are symptoms and laboratory findings suggestive of the post-hepatitis syndrome. *R. Schneider*

714. **Electrolyte Losses with Biliary Fistula: the Post-choledochostomy Acidotic Syndrome**
M. H. Cass, B. Robson, and F. F. Rundle. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 165–169, Feb. 5, 1955. 3 figs., 9 refs.

INTESTINES

715. **Ileocecal Valve Syndrome**
E. C. Lasser and L. G. Rigler. *Gastroenterology* [*Gastroenterology*] **28**, 1–16, Jan., 1955. 12 figs., 14 refs.

Enlargement of the ileo-caecal valve was demonstrated radiologically at the University of Minnesota Hospitals, Minneapolis, in an [unspecified] number of barium-enema examinations during a 4-year period on 18 patients suffering from right-sided abdominal pain and tenderness. In no case was the enlargement confirmed at operation, surgical intervention not being regarded as justifiable in such cases. The clinical and radiological features of 9 of the 18 cases are briefly described. [It is not easy to see the relation between their symptoms and the enlarged valve.] Two of these 9 patients subsequently died from unrelated causes but unfortunately at the post-mortem examination the attention of the pathologist "was not directed to the valve". No abnormalities were observed in the gastro-intestinal tract in either case.

Denys Jennings

716. **Non-specific Enterocolitis**
W. T. Cooke and B. N. Brooke. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **24**, 1–22, Jan., 1955. 8 figs., bibliography.

From the Queen Elizabeth Hospital, Birmingham, a group of 13 cases is reported in which there was evidence of small-bowel and colonic inflammatory disease which differed clinically from that seen in such conditions as ulcerative colitis with secondary involvement of the ileum or regional ileitis spreading into the caecum and colon. The suggestion is put forward that the signs and symptoms in these cases may represent a syndrome *sui generis*.

Diarrhoea was the presenting feature in all cases and blood and mucus were often present in the stools but usually in microscopic amounts only, in contrast to those of ulcerative colitis. In all except 2 cases there was an excessive amount of fat in the stools, indicating small-intestine involvement; further evidence of the latter was found in the radiological changes in the small intestine in 10 cases, at operation in 2, and at necropsy in one case. The fat excretion varied from 4 to 40 g. daily on an intake of 50 g. The macroscopic appearance of the small intestine showed oedema, usually greatest in the lower ileum, with shallow ulcers in the ileum and caecum. The picture was complicated in 2 of the 4 cases in which the bowel could be inspected by the presence of an ileo-transverse anastomosis in one and a carcinomatous stricture of the colon in the other. The radiological changes included both delayed and increased speed of transit of a barium meal; a deficiency pattern, "moth-eaten" and dilated intestine, and "saw-tooth" irregularity of the mucosal outline were reported in some cases. In contradistinction to regional ileitis, stricture of the terminal ileum was observed only once—in a case in which there had been dilatation in this region previously.

Radiological evidence of involvement of the colon was found in all cases examined; the appearances were usually indistinguishable from those of ulcerative colitis, pseudopolyposis being observed in some instances. Sigmoidoscopy revealed no abnormality in 2 cases, slight changes in 2, and changes suggestive of those seen in ulcerative colitis in the remainder.

Of the 13 patients, 7 died; others appeared to have complete remission of symptoms. In one case the radiological picture became normal over a period of 4 years. The caecum and ascending colon were chiefly involved and the condition improved distally.

The danger of ileostomy in cases of disease of the small intestine is stressed.

[There may not be general agreement that the evidence justifies grouping these cases in a specific category, but all who are interested in the confusing picture presented by non-specific inflammatory disease of the small intestine should read this interesting paper in the original.]

T. D. Kellock

717. **A Trial of Intravenous Trypsin in the Treatment of Chronic Ulcerative Colitis**
F. Milanés, J. Piedra, and E. Morales. *Gastroenterology* [*Gastroenterology*] **28**, 110–117, Jan., 1955. 4 refs.

Trypsin given intravenously in a case of ulcerative colitis complicated by thrombosis of the right popliteal vein had such a beneficial effect on the colitis that a further clinical trial of the drug was considered worth while. At the Garcia University, Havana, trypsin was given in 7 cases (including the original one) of ulcerative colitis of some years' duration, intravenously in 5 cases and intramuscularly in 2. In 5 of the 7 patients there was considerable improvement in the colitis, although in 4 of those receiving intravenous therapy there were marked side-effects, in spite of administration of antihistamine drugs by mouth. In the original case improvement was sudden and dramatic 3 weeks after the course of trypsin.

The authors [rightly] stress the indefinite nature of the results and the marked side-effects. *T. D. Kellock*

Cardiovascular System

718. **The Cardiovascular Aspects of Marfan's Syndrome: a Heritable Disorder of Connective Tissue**
V. A. McKusick. *Circulation* [*Circulation (N.Y.)*] **11**, 321–342, March, 1955. 11 figs., bibliography.

Marfan's syndrome is characterized by a wide variety of abnormalities which may be present in different combinations. The commonest abnormality is congenital dislocation of the lens, others being unusual length of limb with poor muscular tone, arachnodactyly, talipes, pes planus or syndactyly, herniae, high-arching palate, and kyphosis causing either pigeon-breast or pectus excavatum.

In this paper from the Johns Hopkins University and Hospital the author discusses the cardiovascular abnormalities. These generally affect the ascending aorta, causing fusiform aneurysm, dissecting aneurysm, and dilatation of the aortic ring with aortic incompetence. Any of these may directly or indirectly cause death, possibly suddenly, in children or young adults. Less commonly there may be minor degrees of coarctation of the aorta, patent ductus, atrial septal defect, dilatation of the pulmonary artery, and mitral-valve deformities, which last may be complicated by bacterial endocarditis. It seems likely that the diagnosis of Marfan's syndrome may be overlooked in cardiac patients in whom the significance of abnormalities elsewhere in the body is not appreciated.

The author suggests that the underlying abnormality in all lesions may be an abiotrophy of connective tissue, causing disruption of elastic fibres which may not become evident until late childhood or adult life. In a study of the familial aspects of the condition he traced 50 families in which there was one certain instance of Marfan's syndrome; in 70% of the families there were other certain or possible cases. The total number of definitely affected subjects was approximately 105, and in 46 of these the cardiovascular system was involved. Illustrative cases are described. *J. A. Cosh*

719. **Effects of Tobacco and Whiskey on the Cardiovascular System**
H. I. Russek, B. L. Zohman, and V. J. Dorset. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **157**, 563–568, Feb. 12, 1955. 5 figs., 12 refs.

The authors' findings in an investigation at the United States Public Health Service Hospital, Staten Island, New York, of the effects of smoking and consumption of alcohol on the cardiovascular system may be summarized as follows. Inhalation of tobacco smoke causes a tachycardia, a rise in blood pressure, depression of the S–T segment in the electrocardiogram, and deterioration of the ballistocardiographic tracing. Consumption of 1 or 2 oz. (28 or 57 ml.) of whisky does not reduce these effects, and although some improvement in the ballistocardiogram is noted, this is considered to reflect the peripheral vasodilator effect of the whisky rather than any improvement in the circulation in the coronary arteries. The fact that the electrocardiogram becomes normal after the subject stops smoking is taken to indicate that patients with evidence of coronary disease should not smoke and that doctors should beware of diagnosing coronary thrombosis in heavy smokers until the effect of abstinence from smoking has been observed.
J. Robertson Sinton

720. **Effect of Cigarette Smoking in the Normal Person**
I. E. Buff. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **157**, 569, Feb. 12, 1955. 1 fig., 6 refs.

The effect of cigarette smoking on the heart was investigated by means of the ballistocardiograph in 400 healthy subjects of both sexes in the age group 20 to 40 years. A decrease in the size of the H, I, J, and K waves and " notching " of the J wave occurred after smoking in 42 subjects, the majority of whom were over 30 years of age. The author considers that all subjects in whom the ballistocardiogram is abnormal should discontinue smoking, but he admits that it will be necessary to follow up a large number for many years before it can justly be concluded that they are more likely to develop coronary thrombosis if they continue to smoke than if they do not.
J. Robertson Sinton

721. **Results of Treatment of Portal Hypertension.** (Опыт лечения больных с портальной гипертензией)
T. O. Koryakina. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **33**, 53–61, Feb., 1955.

Since June, 1952, 22 patients with portal hypertension have been investigated at the Surgical Clinic of the Pavlov Institute of Medicine, Leningrad, of whom 14 underwent operation, porta-caval anastomosis being performed in 7 cases, spleno-renal anastomosis in 3, and mesenterico-caval anastomosis in 2; while in the remaining 2 cases an anastomosis could not be established. The portal hypertension was attributed to the effects of infective hepatitis in 7 cases, to alcoholic cirrhosis in 3, to syphilis in 3, and to Wilson's disease (hepatolenticular degeneration), splenic thrombosis, and cavernoma of the liver in one case each; in 6 cases the cause could not be established. Massive haematemesis or melaena was the presenting symptom in 12 cases and was followed by ascites, which disappeared after restoration to normal of the blood protein and haemoglobin levels. In those cases in which ascites was not preceded by haemorrhage it was more persistent.

Surgical relief of portal hypertension is indicated in cases of haemorrhage from oesophageal varices and of ascites not associated with anaemia or hypoproteinaemia (or rather, not controlled by the restoration of normal blood protein and haemoglobin levels). A full investigation of liver and kidney function and of the coagulation

mechanism of the blood should be undertaken before operation, which is contraindicated if the prothrombin time is less than 30% of normal. In some cases transparietal portal angiography may be of value. Preparation for operation should be prolonged and designed to restore liver function by such measures as intravenous glucose, large doses of vitamins B, C, and K, serum or blood transfusions, and a high-protein diet. If the total serum protein level is not substantially raised by such a regimen, this is a further contraindication to operation, as also are a serum albumin content of less than 3 g. per 100 ml. or an albumin:globulin ratio of less than 0·8 and a reduced sugar tolerance.

Operation in the author's cases was carried out under cover of penicillin, streptomycin being added subsequently, and dicoumarol was given for 24 hours before and after operation. There were 4 postoperative deaths, 2 from coma, one from oesophageal haemorrhage, and one from portal venous thrombosis. The remaining cases were successfully relieved of haematemesis and ascites, although the underlying hepatic disease continues to progress. No final conclusions can yet be drawn as to the ultimate prognosis of portal hypertension treated by porta-caval anastomosis.

L. Firman-Edwards

722. **The Interrelations of the Pulmonary Arterial and Venous Wedge Pressures**

R. H. WILSON, W. HOSETH, and M. DEMPSEY. *Circulation Research* [*Circulat. Res.*] **3**, 3–6, Jan., 1955. 5 figs., 2 refs.

A pressure recorded through a cardiac catheter wedged in a pulmonary artery may be referred to as a " pulmonary arterial wedge pressure ". Similarly, the pressure recorded through a catheter wedged in a pulmonary vein during thoracotomy, or in animals, has been called a " pulmonary venous wedge pressure ".

Studies on dogs carried out at the Southwestern Medical School of the University of Texas showed that pulmonary arterial wedge pressure was closely correlated with mean left atrial pressure, and pulmonary venous wedge pressure with mean pulmonary arterial pressure. Such findings indicate very low " resistance " in the pulmonary capillaries in normal dogs. *J. McMichael*

MYOCARDIUM

723. **Acute, Fatal Myocarditis. Clinical-pathological Analysis of 15 Cases of Fatal Myocarditis and Some Diagnostic and Therapeutic Considerations.** [In English]

K. GYDELL, G. BIÖRCK, and S. WINBLAD. *Acta medica Scandinavica* [*Acta med. scand.*] **151**, 1–17, Feb. 8, 1955. 28 refs.

The clinical features and necropsy findings in 15 cases of myocarditis, seen for the most part at Malmö General Hospital, Sweden, between 1944 and 1952, were analysed. The cases were divided into two groups according to the necropsy findings: (1) rheumatic myocarditis, in which Aschoff granulomata were found (7 cases); and (2) non-rheumatic myocarditis, in which non-specific inflammatory changes were noted (8 cases). Cardiac enlargement was present in all except 2.

Fatigue and dyspnoea were prominent symptoms; tachycardia was observed in 12 cases and there was clinical evidence of cardiac enlargement in 7. In most cases blood pressure was within the normal range; it was persistently low in only 2 cases. The erythrocyte sedimentation rate was raised and leucocytosis was present in all cases for which adequate clinical records were available. The most frequent electrocardiographic changes were abnormalities in the S–T segment and T waves. In several of the cases of non-rheumatic myocarditis the condition was not diagnosed during life. The authors point out that in these cases sudden death may follow an apparently mild infection of the respiratory tract, such infection being apparently the commonest associated cause of death.

It is believed that the incidence of acute myocarditis is decreasing, perhaps as the result of the use of antibiotics in respiratory infection; if, however, such an infection does not respond to antibiotics the possibility of myocarditis as a complication should be considered, and serial radiographs and electrocardiograms should be examined. Rheumatic myocarditis is generally more readily diagnosed than the non-rheumatic form because the patient's history is suggestive. The authors advise retaining the term myocarditis for a wide variety of infections and hyperergic, allergic, toxic, and metabolic conditions in order to emphasize the " structural lesions of myocardial cells " (apart from ischaemic heart disease) " resulting in impairment of cardiac function ".

R. S. Stevens

724. **Ventricular Function. VII. Changes in Coronary Resistance and Ventricular Function Resulting from Acutely Induced Anemia and the Effect Thereon of Coronary Stenosis**

R. B. CASE, E. BERGLUND, and S. J. SARNOFF. *American Journal of Medicine* [*Amer. J. Med.*] **18**, 397–405, March, 1955. 5 figs., 20 refs.

At Harvard School of Public Health, Boston, the response of the coronary vessels to anaemia was studied in dogs under morphine–chloralose–urethane anaesthesia. After the performance of a high cervical vagotomy and with the chest open, the blood flow in the left main coronary artery, the cardiac output, and the right and left atrial and pulmonary arterial and aortic pressures were continuously recorded, coronary resistance and ventricular work being then calculated from these findings. The dogs were first observed in a control state and later under varying degrees of anaemia produced by replacement of the blood by dextran solution.

During anaemia a greater coronary arterial blood flow per unit of left ventricular work was observed, as well as an increased removal of oxygen from the blood passing through the cardiac muscle, so that by these means the decreased oxygen-carrying capacity of the blood was to some extent compensated for. It was observed that at a haematocrit value of between 24 and 31% depression of the curve of ventricular function began to appear and it is assumed that at this stage the coronary vessels were

fully dilated and could not further compensate for the decreased oxygen-carrying capacity of the blood. At high work loads and with a normal haematocrit value, however, a substantial vasodilatory reserve was still present, indicating that in these circumstances maximum ventricular work is not limited by availability of oxygen. When coronary stenosis was produced experimentally, depression of ventricular function occurred, and this depression was accentuated by the presence of anaemia.

H. E. Holling

CHRONIC VALVULAR DISEASE

725. **Causes of Death in Rheumatic Heart Disease. Relationship to the Incidence of Mitral Stenosis Occurring Alone or with Other Valvular Lesions**

L. A. SOLOFF and J. ZATUCHNI. *American Journal of Medicine* [*Amer. J. Med.*] **18**, 419–427, March, 1955. 10 refs.

The causes of death in 141 cases at Temple University and Episcopal Hospitals, Philadelphia, in which rheumatic heart disease was diagnosed clinically were analysed, with special reference to the incidence of mitral stenosis. The causes of death were heart failure (39·7%), acute carditis (13·5%), bacterial endocarditis (11·3%), systemic embolism with pre-existing heart failure (9·2%), systemic embolism without failure (8·5%), and pulmonary infarction (6·4%). In the remainder death was not related to rheumatic heart disease or its sequelae. The authors point out that an analysis based on deaths only is a form of selection, since " it is the persons who die earliest—that is, the poorest risks, who are used to determine prognosis figures ". Mitral stenosis in combination with other valvular lesions was about twice as common as isolated mitral stenosis. A clinical diagnosis of isolated mitral-valve disease was made in 49·7% of the cases, but was confirmed at necropsy in only 26·1%, this error in the clinical diagnosis being most frequent in patients who died from congestive failure. Calcification of the mitral valve was found at necropsy in 13% of cases, but not as an isolated valvular lesion.

James W. Brown

726. **The Use of Simultaneous Left Heart Pressure Pulse Measurements in Evaluating the Effects of Mitral Valve Surgery**

H. L. MOSCOVITZ, A. J. GORDON, E. BRAUNWALD, S. S. AMRAM, S. O. SAPIN, R. P. LASSER, A. HIMMELSTEIN, and M. M. RAVITCH. *American Journal of Medicine* [*Amer. J. Med.*] **18**, 406–414, March, 1955. 5 figs., 35 refs.

During the operation of mitral valvotomy on 7 patients at Mount Sinai Hospital, New York, the pressure gradient across the stenosed mitral valve was determined by simultaneous measurement of the left atrial and left ventricular pressures, No. 20 needles being inserted into the left atrium, the left ventricle, and the aorta and being connected to three matched strain-gauge manometers by sterilized vinyl tubing.

The difference in filling pressure across the healthy mitral valve is normally too small to be measurable, but when the valve is stenosed the pressure gradient may rise to 20 mm. Hg. A more accurate assessment of the changes in filling pressure under different conditions would be aided by the simultaneous measurement of cardiac output, but so far the authors have not found it possible to do this under the conditions obtaining in the operating theatre. They point out that the performance of valvotomy is accompanied by a reduction in the pressure gradient which is correlated with the adequacy of the surgical procedure. In all cases the reduction in the pressure gradient is mainly due to a reduction in left atrial pressure, but in a few cases an elevation of left ventricular diastolic pressure also occurs. The authors suggest that measurement of the pressure gradient during the course of a valvotomy provides an estimate of the likely extent of the residual stenosis and is thus of help in deciding whether the attempt to increase the valve opening should be continued.

H. E. Holling

MYOCARDIAL INFARCTION AND CORONARY DISEASE

727. **Experimental Infarction of the Ventricular Myocardium.** (К вопросу об экспериментальном инфаркте миокарда желудочков сердца)

A. E. SMIRNOV and A. E. SHUMILINA. *Клиническая Медицина* [*Klin. Med.* (*Mosk.*)] **33**, 62–77, Feb., 1955. 6 figs., 2 refs.

To ascertain the effect of stimulation of the vagus nerves on the heart in conditions of coronary insufficiency, the authors performed two series of experiments on dogs at the Institute of Pharmacology of the Academy of Medical Science, Moscow. In the first series acute occlusion of the left coronary artery was produced under morphine–urethane narcosis and artificial respiration. In 30% of cases extrasystoles occurred at some stage, and 2 of the animals developed ventricular fibrillation and died. Changes in the electrocardiogram (chiefly an increase in T_2 and T_3) developed in most cases 2 to 10 minutes after occlusion of the artery, but in rare cases they did not occur until 4 or more hours later, while in one case continuous extrasystoles developed only after 32 hours. The great variability of the time of onset of these changes is explained by the authors as being due to variations in the vascularity of the heart and in the adequacy of collateral circulation. In those animals which survived the operation for one or more hours the contractile force of the ventricles was increased, as in normal dogs, by vagal stimulation. After stimulation had continued for 20 to 30 minutes, however, the heart began to dilate, its elasticity diminished, and death occurred. Post mortem the heart muscle was flabby, while massive haemorrhages were found under the epicardium and endocardium and there were widespread foci of degeneration in the myocardium. No such changes were found in the hearts of dogs not subjected to vagal stimulation.

In the second series of experiments a more gradual occlusion of the left coronary artery was produced. Those dogs which survived the immediate effects began

to recover after 3 days, and by the end of 10 days there was little to distinguish them from control animals except that they tired easily and kept lying down and that most of them had continuous extrasystoles. Section of both vagus nerves suppressed the extrasystoles in these animals, while stimulation of the distal ends of the cut nerves caused their temporary reappearance.

It is therefore concluded that vagal activity after either sudden or gradual coronary occlusion aggravates the cardiac condition in experimental animals. Discussing the clinical implications of these findings, the authors suggest that it is important in cases of coronary occlusion to shield the heart from excessive vagal activity by avoiding all circumstances which may upset the functional equilibrium between the cerebral cortex and the subcortical centres, and to suppress vagal activity by means of atropine or other drugs if bradycardia or other evidence of such activity is observed.

L. Firman-Edwards

728. **Anticoagulant Treatment of Cardiac Infarction.** (Zur Antikoagulantientherapie des Herzinfarktes)
W. LÖFFLER and M. SCHNEBLI. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **80**, 305–308, March 4, 1955. 1 fig.

The patient who is admitted to hospital having survived the initial hazards of cardiac infarction runs a great risk of dying of thrombo-embolic complications during the next few weeks—a risk estimated by the present authors to be one in three. There is therefore *a priori* a strong case for treating such patients with anticoagulants, and the authors compare the fate of 200 patients so treated at the University Medical Clinic, Zürich, with that of 100 others who were not given anticoagulants. They admit that the two groups may not have been strictly comparable, but when 17 treated patients aged 60 to 70 years were matched individually against 17 untreated patients the findings confirmed those of the study as a whole. Mortality in the treated group was 24%, compared with 73% in the untreated. Systemic and pulmonary embolism were about 8 times more frequent amongst untreated cases. Secondary cardiac infarction was apparently not prevented by treatment, though 10 of 14 patients in the treated group survived its occurrence, whereas all of 5 untreated patients died. There was a higher incidence of complications in inadequately treated patients.

The following scheme of treatment is recommended. Dicoumarol is given to all patients, 18 mg. on the first day, 6 to 9 mg. on the second, and 1·5 to 4·5 mg. thereafter; heparin may not be necessary when infarction has occurred very recently and should never be given intramuscularly. The prothrombin activity should be reduced to about 20% of normal (Quick's method) and strictly controlled. Using this scheme, the authors observed few complications: mild bleeding occurred in 6% of the patients, serious haemorrhage in one case, and allergic arteritis in one case.

The authors consider that all patients with cardiac infarction should be treated with anticoagulants unless definite contraindications. such as a bleeding tendency or peptic ulcer, exist. They reject the distinction between " good-risk " and " bad-risk " cases, pointing out that a patient placed initially in the former category may rapidly pass into the latter category.

[The value of this trial is unfortunately greatly reduced by the lack of the clinical details necessary to enable the treated and untreated cases to be compared; nor, indeed, can the type of patient treated be judged. The absolute interdiction of intramuscular heparin will strike many physicians in Great Britain as somewhat curious.]

F. Starer

729. **Revascularization of the Heart by Pedicled Skin Flap. An Experimental Study Investigating the Functions of Extra-coronary Anastomoses**
J. VON WEDEL, J. W. LORD, C. G. NEUMANN, and J. W. HINTON. *Surgery* [*Surgery*] **37**, 32–53, Jan., 1955. 10 figs., 46 refs.

730. **Objective Evaluation of Coronary Vasodilator Drugs**
H. I. RUSSEK, B. L. ZOHMAN, and V. J. DORSET. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **229**, 46–54, Jan., 1955. 4 figs., 10 refs.

The efficacy of supposed coronary vasodilator drugs was studied at the United States Public Health Service Hospital, Staten Island, New York, by observing whether they modified the electrocardiographic response to a standard Master two-step exercise test. The ability of these drugs to relieve pain on exertion was not primarily considered. The patients selected included 60 with coronary disease in whom, on repeated testing under identical conditions, there was a relatively constant positive electrocardiographic response to exercise which could be favourably modified by a sublingual dose of glyceryl trinitrate taken just before the test (glyceryl trinitrate being accepted as a potent coronary vasodilator). Of all the drugs tried, only two in addition to glyceryl trinitrate gave responses which justified their use in the management of angina pectoris. Thus papaverine, 1 to 2 gr. (0·06 to 0·13 g.) intravenously or 3 to 8 gr. (0·2 to 0·52 g.) by mouth, was effective in 14 out of 24 patients, but was ineffective in the usual therapeutic dosage. The only drug which was of any value for more prolonged prophylaxis was pentaerythrityl tetranitrate (" peritrate "), 10 to 20 mg. having a marked effect for 4 to 5 hours by this test. In contrast to the standard preparation, " nitroglyn ", which in tablet form contains specially coated granules of glyceryl trinitrate, was relatively ineffective even in a dose as high as 4/25 gr. (10·4 mg.). Little or no effect was obtained with triethanolamine trinitrate biphosphate (" metamine "), dioxyline phosphate (" paveril "), aminophylline (theophylline), " roniacol ", tolazoline hydrochloride (" priscoline "), tetraethylammonium chloride, octyl nitrite, khellin, heparin, dicoumarol, or morphine. Ethyl alcohol consistently failed to modify the electrocardiogram on exercise, even though it often reduced the anginal pain. Like morphine, therefore, it is a sedative, not a coronary vasodilator, and there may be a danger in using it since its peripheral vasodilator action may

induce compensatory vasoconstriction elsewhere. The authors did not observe any striking subjective improvement in anginal symptoms in response to heparin.

J. N. Agate

731. **Postmortem Studies on Coronary Atherosclerosis, Serum Beta Lipoproteins and Somatotypes**

D. M. SPAIN, V. A. BRADESS, and I. J. GREENBLATT. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **229**, 294–301, March, 1955. 6 figs., 4 refs.

In continuation of a previous investigation (*Ann. intern. Med.*, 1952, **38**, 254; *Abstracts of World Medicine*, 1953, **14**, 216) the authors have carried out, at the Beth-El Hospital, Brooklyn, New York, a post-mortem study of the relationship between the serum beta-lipoprotein level, the somatotype of the patient, and the degree of coronary atherosclerosis in 157 apparently healthy persons who died suddenly from accident, suicide, homicide, or coronary occlusion; somatotypes were determined according to Sheldon's methods. In most of the cases blood for analysis was obtained within 6 hours after death.

Of the 157 subjects, 73 died suddenly from coronary accident, and in 58 of these there was an abnormal beta-lipoprotein pattern. The over-all coefficient of correlation between the serum beta-lipoprotein pattern and the degree of coronary atherosclerosis was 0·84. When the cases were classified by somatotype the correlation for the mixed group of mesomorphs and endomorphs was 0·91, whereas for the group consisting of ectomorphic males it was only 0·6. The authors conclude from this study that " any male or female, with the exception of the ectomorphic male, who has an abnormal serum beta-lipoprotein pattern must be seriously regarded as a potential victim of atherosclerosis. This is particularly true of the mesomorphic male ".

Z. A. Leitner

HEART FAILURE

732. **Effects of Valsalva's Manœuvre on the Normal and Failing Circulation**

E. P. SHARPEY-SCHAFER. *British Medical Journal* [*Brit. med. J.*] **1**, 693–695, March 19, 1955. 5 figs., 13 refs.

In this paper the author describes the effects produced on the circulation by performance of the Valsalva manœuvre, as observed at St. Thomas's Hospital, London, in 62 healthy subjects and 63 patients with heart failure of varied aetiology.

In normal subjects the Valsalva manœuvre produces a rise in intrathoracic pressure which causes a decrease in the effective filling pressure of the heart. Continuous records of the arterial pressure, taken with capacitance manometers, show that there is a decrease in both mean and pulse pressures during the manœuvre, followed on its completion by a sharp rise in diastolic pressure (the " overshoot ") which is thought to be due to a baroceptor response to the fall in pulse pressure during the manœuvre. The rate at which the blood pressure falls is dependent on the initial state of vasomotor tone, being greatest where this is low—for example, in thyrotoxicosis. There is a direct relation between the maximum percentage change in pulse pressure during the Valsalva manœuvre and the maximum change in diastolic pressure during the " overshoot ".

Patients in heart failure with normal rhythm show two types of response. In the majority there is no change in pulse pressure during the Valsalva manœuvre and therefore no subsequent " overshoot "—the so-called " square-wave " pattern—the failing heart being unable to alter its stroke volume in response to a rapid fall in filling pressure. In a smaller group there is an increase in pulse pressure during the manœuvre followed by a decrease, indicating vasodilatation. The cases in this group are clinically the more severe, and it is suggested that in them the relation between filling pressure and cardiac output is represented by the falling limb of Starling's curve, the heart responding to a decreased filling pressure by increasing its stroke output and pulse pressure.

The author's findings confirm the theory that a decrease in pulse pressure produces vasoconstriction and an increase in pulse pressure vasodilatation, and show that this is the case in both the normal and the failing circulation, provided the nervous pathways subserving the baroceptor reflexes are intact. The manœuvre can thus be used clinically to detect the presence of heart failure in difficult cases by feeling the pulse during its performance. It is also possible to tell by auscultation during the manœuvre whether a murmur arises from the right or left side of the heart, as a murmur from the right side will reappear immediately on its completion, whereas the return of a left-sided murmur will be delayed for a few beats. This physical sign has limited value, however, because it is present only if the heart responds to the manœuvre in a normal manner.

A. Paton

733. **Diuretic Action of Benemid. Its Effect upon the Urinary Excretion of Sodium, Chloride, Potassium and Water in Edematous Subjects**

D. BRONSKY, A. DUBIN, and D. S. KUSHNER. *American Journal of Medicine* [*Amer. J. Med.*] **18**, 259–266, Feb., 1955. 5 figs., 27 refs.

In this paper from Cook County Hospital and the Northwestern University Medical School, Chicago, the authors describe an investigation into the effect of probenicid (" benemid ") on the urinary excretion of water, sodium, chloride, and potassium and on the concentration of electrolytes in the serum in 26 patients, all of whom were oedematous with the exception of one patient with compensated organic heart disease. [Although it is stated that " subjects with edema due primarily to causes other than congestive heart failure were excluded ", 2 subjects with " cirrhosis and normal cardiac status " are listed among the 25 oedematous patients.] All the patients were kept in bed, and " all except one were completely digitalized ". [Presumably digitalis was also omitted in the 2 cases mentioned above.] No mercurial diuretics were administered for 5 days before the study, during which water was allowed *ad libitum* (but intake was measured) and a low-sodium diet was given. This preliminary observation period enabled subjects in whom

spontaneous diuresis occurred to be excluded. Biochemical investigations were started only after it was ascertained that the clinical status, oedema, weight, and urinary output had become stabilized. The test period consisted of 2 days of control observation, 3 successive days during which probenicid was administered by mouth in a dosage of 4 g. daily, and 1 or 2 subsequent control days. All urine was collected and the concentration of electrolytes in urine and serum was determined daily.

It was found that a significant diuretic effect of probenicid could be observed in respect of water, sodium, and chloride excretion in all of 13 subjects with congestive heart failure uncomplicated by hepatic or renal disease and without electrolyte disturbances, the mean amount of water excreted on the day of maximum response exceeding the mean daily output in the control period by 1,330 ml., that of sodium by 91 mEq., and that of chloride by 76 mEq. One patient with congestive heart failure associated with gout and renal disease showed a lesser, but still significant, response. The maximum diuresis occurred in most instances on either the first or second day of administration of probenicid. Water diuresis without enhancement of sodium or chloride excretion occurred in 7 other subjects, most of whom had had low urinary sodium and chloride concentrations during the control period. The remaining 5 subjects, in whom no diuresis occurred, comprised the one patient without oedema, one with hepatic cirrhosis, 2 with heart failure complicated by renal disease, and one with low sodium excretion during the control period. The long-term toxicity of probenicid in high dosage remains to be determined, but in contrast with the experience of others the authors found that probenicid in the dosage used gave rise to no gastrointestinal distress or other side-effects. It is postulated that probenicid-induced diuresis is the result of decreased tubular reabsorption of water, sodium, and chloride.

E. Forrai

HYPERTENSION

734. **Treatment of Hypertension with Oral Reserpine Alone and in Combination with Hydralazine or Hexamethonium**

W. M. HUGHES, E. DENNIS, and J. H. MOYER. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **229**, 121–134, Feb., 1955. 5 refs.

Reserpine alone or combined with hydrallazine or hexamethonium bromide was given to 73 out-patients at the Jefferson Davis Hospital, Houston, Texas, who were suffering from mild to severe hypertension. To 6 patients who required rapid and effective treatment reserpine combined with either hexamethonium or hydrallazine was given from the start. Of the remaining 67 patients, all of whom received reserpine alone initially, 8 became normotensive and remained so for a follow-up period of one year, and 18 for various reasons were not given added hexamethonium or hydrallazine. Altogether 41 patients received reserpine combined with hydrallazine or hexamethonium after 2 months' treatment with reserpine alone in a maintenance dosage of 2 mg. a day, and 6 received combined therapy from the beginning. The results were as follows.

Of 15 patients treated with reserpine and hydrallazine, 7 had been responsive to reserpine alone and in 6 of these there was a further blood-pressure response to hydrallazine. A satisfactory fall in blood pressure was also observed in 6 out of 7 patients on whom reserpine had no effect. One patient given both drugs from the outset was quite unresponsive. A satisfactory blood-pressure response was thus obtained in 13 of these 15 patients, 5 becoming normotensive. The dosage of hydrallazine, varied from 100 to 800 mg. a day (average 331 mg. a day). Of 32 patients given reserpine and hexamethonium, 6 had responded to reserpine alone, and in 4 of these there was a further fall in blood pressure with hexamethonium. Of 21 patients on whom reserpine had had no effect alone, 18 responded to hexamethonium. In the remaining 5 patients who received reserpine and hexamethonium from the outset there was a satisfactory fall in blood pressure. Thus a satisfactory blood-pressure response was noted in 24 of this group of 32 patients, 15 becoming normotensive. The dose of hexamethonium varied from 0·5 to 4 g. a day (average 1·4 g.).

Symptomatic improvement, particularly relief of headache, angina, and congestive heart failure, was most marked in patients given reserpine and hexamethonium. Side-effects were less frequent and severe with combined therapy than with hydrallazine or hexamethonium alone for comparable falls in blood pressure. Estimation of the glomerular filtration rate and renal blood flow in 11 cases revealed no significant improvement despite successful reduction in blood pressure. *K. G. Lowe*

735. **The Effect of Blood Pressure Reduction with Arfonad on Renal Hemodynamics and the Excretion of Water and Electrolytes in Patients with Hypertension**

J. H. MOYER, R. MCCONN, and R. A. SEIBERT. *American Heart Journal* [*Amer. Heart J.*] **49**, 360–366, March, 1955. 7 refs.

At Baylor University College of Medicine, Houston, Texas, " arfonad " (D-3:4-(1:3′-dibenzyl-2′-ketoimidazalido)-1:2:trimethylene thiophanium D-camphor sulphonate) was administered by continuous intravenous infusion to 8 patients with fixed hypertension at a rate of 1 to 10 mg. per minute for periods of 2 to 3 hours. The mean blood pressure fell from an average of 143 to 91 mm. Hg. The mean renal blood flow fell at first, but at the end of 2 hours it was above the control level owing to a fall in renal vascular resistance. The glomerular filtration rate was depressed during the whole hypotensive episode and there was a concomitant fall in urine volume and in sodium, but not potassium, excretion. Side-effects, chiefly nausea, extreme weakness, and restlessness, were noted in 4 patients. *K. G. Lowe*

736. **The Effect of Intravenous Protoveratrine on Digital Pulse Volume and Digital Skin Temperature in Hypertensive Patients**

J. H. CURRENS, J. F. MCGINTY, R. B. KHAMBATTA, and I. GORDON. *Circulation* [*Circulation (N.Y.)*] **11**, 440–446, March, 1955. 5 figs., 16 refs.

Haematology

737. **Splenic Aspiration in Clinical and Experimental Hematology**
R. J. WATSON, H. D. SHAPIRO, R. R. ELLISON, and H. C. LICHTMAN. *Blood* [*Blood*] **10**, 259–271, March, 1955. 15 figs., 12 refs.

The findings obtained by the study of splenic aspirations in 140 patients are presented. Diagnostically they were most helpful in myeloid metaplasia, lymphoma, kala-azar, and Gaucher's disease. The findings were of particular theoretical interest in multiple myeloma and sickle cell anemia. This method of investigation could be extended to elucidating further the role of the spleen in other diseases. No morbidity was encountered in this series. If certain precautions are observed, splenic puncture is a safe procedure, and should be undertaken in patients with undiagnosed splenomegaly.—[Authors' summary.]

HAEMORRHAGIC DISEASES

738. **Plasma Thromboplastin Antecedent (PTA) Deficiency: Clinical, Coagulation, Therapeutic and Hereditary Aspects of a New Hemophilia-like Disease**
R. L. ROSENTHAL, O. H. DRESKIN, and N. ROSENTHAL. *Blood* [*Blood*] **10**, 120–131, Feb., 1955. 2 figs., 29 refs.

The authors describe a new haemorrhagic disorder which is apparently distinct from haemophilia due to lack of antihaemophilic globulin (haemophilia A) and Christmas disease (haemophilia B) due to lack of plasma thromboplastin component (P.T.C.). A preliminary report on this condition has been published elsewhere (*Proc. Soc. exp. Biol.* (*N.Y.*), 1953, **82**, 171; *Abstracts of World Medicine*, 1953, **14**, 223). In addition to the 3 patients originally studied, investigations have now been carried out on 10 other members of the same family, distributed through 4 generations. In all, 6 of the 13 members of the family examined had, to a variable degree, a haemorrhagic tendency. The inheritance is of interest in that both males and females are affected and that transmission is as an autosomal dominant trait with a probable high degree of penetrance and variable expression of the gene. It appears that the disease can be transmitted by either sex to both male and female offspring.

The clinical severity of the haemorrhagic tendency in these patients was very much less than in most cases of haemophilia and Christmas disease. They rarely developed spontaneous bleeding, excessive haemorrhage usually only following trauma or a surgical procedure. Haemarthrosis was rare. Laboratory investigations of the blood of those affected showed there to be a deficiency of plasma thromboplastin antecedent (P.T.A.). The whole-blood clotting time was slightly prolonged in some cases and there was some degree of impairment of prothrombin utilization. The one-stage "prothrombin" time, tourniquet test, bleeding time, and platelet count were all normal. Blood from these patients corrected the deficiency in haemophilia and Christmas disease.

The properties of P.T.A. are compared with those of antihaemophilic globulin and of P.T.C. Antihaemophilic globulin is used up during the clotting of normal blood and therefore none is found in normal serum, whereas P.T.A. (like P.T.C.) is not consumed during clotting and therefore is present in serum. P.T.A. (like antihaemophilic globulin) is not adsorbed on to barium sulphate, whereas P.T.C. is so adsorbed. P.T.A. (like P.T.C.) does not disappear on storage as does antihaemophilic globulin.

[This is a paper of importance to those interested in blood coagulation. It is probable that this condition could be detected by means of the thromboplastin generation technique, using the patient's adsorbed plasma and patient's serum together in the incubation mixture.]

A. S. Douglas

739. **Alpha-prothromboplastin Deficiencies (Haemophilia) of Differing Degrees in a Mother and Son**
P. FANTL and J. MARGOLIS. *British Medical Journal* [*Brit. med. J.*] **1**, 640–642, March 12, 1955. 2 figs., 13 refs.

A congenital haemorrhagic tendency of moderate severity in a mother was shown to be due to a partial alpha-prothromboplastin deficiency (haemophilia) in her blood. Her daughter has no bleeding tendency. The son is a very severe bleeder. His blood is completely devoid of alpha-prothromboplastin. Puzzling genetic features in the presented cases are pointed out.—[Authors' summary.]

ANAEMIA

740. **A-B Hemolytic Disease of the Newborn. Analysis of 1,480 Cord Blood Specimens, with Special Reference to the Direct Antiglobulin Test and to the Group O Mother**
R. E. ROSENFIELD. *Blood* [*Blood*] **10**, 17–28, Jan., 1955. 27 refs.

Samples of cord blood from 1,486 babies born at the Mount Sinai Hospital, New York, were examined, the blood group and compatibility with maternal blood being determined and the direct antiglobulin test performed in each case. In 1,127 cases the haemoglobin content was determined, in 1,112 cases the reticulocytes were counted, and in 929 cases the plasma bilirubin level was estimated. In cases of group incompatibility the mother's serum was tested for immune A and B antibodies and haemolysins.

A weakly positive response to the antiglobulin test was found in 39, or more than 11%, of the babies whose blood

group was incompatible with that of the mother, whereas the result was never positive when the groups were compatible. The babies giving a weakly positive antiglobulin reaction appeared to form an abnormal group since the mean haemoglobin content of their blood was lower, mean reticulocyte count higher, and mean serum bilirubin level higher than those of other infants with group incompatibility. A striking finding was that 38 of the mothers of the 39 infants in this group were of Group O, while increased osmotic fragility of the erythrocytes was found in 31 of these infants.

John Murray

741. **Evaluation of the Quantitative Direct Antiglobulin Test in Hemolytic Disease of the Newborn Due to Anti-D**
T. J. GREENWALT and J. A. WAGNER. *Blood* [*Blood*] **10**, 29–34, Jan., 1955. 1 fig., 15 refs.

In 86 infants suffering from haemolytic disease due to anti-D iso-immunization no correlation could be demonstrated between the strength of reaction in the antiglobulin test and the clinical severity. *John Murray*

742. **Cooley's Anaemia in Children in Indonesia.** [In English]
LIE-INJO LUAN ENG and JO KIAN TJAY. *Documenta de medicina geographica et tropica* [*Docum. Med. geogr. trop. (Amst.)*] **7**, 30–42, March, 1955. 8 figs., 15 refs.

743. **The Hematopoietic and Goitrogenic Effects of Cobaltous Chloride in Patients with Sickle Cell Anemia**
R. T. GROSS, J. P. KRISS, and T. H. SPAET. *Pediatrics* [*Pediatrics*] **15**, 284–290, March, 1955. 5 figs., 13 refs.

The value of cobaltous chloride in sickle-cell anaemia is discussed on the basis of the results obtained at Stanford University School of Medicine, San Francisco, in 4 children (3 males and one female) aged 4 to 12 years who were severely anaemic and had been observed for periods of 15 months to 7 years before institution of cobalt therapy. The dosage of the drug, which was given by mouth in the form of enteric-coated capsules, was not constant for all the patients, but was generally 2 mg. per kg. body weight daily at the start, rising to 4 mg. per kg. daily over a period of about 6 months; the oldest patient at the end of treatment was receiving 8 mg. per kg. daily. Progress was assessed clinically by the occurrence of sickling crises and secondary infection. The haematopoietic response was judged from the results of serial determinations of the haemoglobin concentration, while thyroid function was estimated from the radioactive-iodine uptake, the level of serum protein-bound iodine, and the serum cholesterol level. Later in the investigation the serum cobalt concentration was determined.

In all the cases there was an initial satisfactory haematopoietic response, although there was no indication of the mechanism whereby cobalt produced this effect. In no case was the presence or distribution of abnormal haemoglobin in any way altered. The incidence of sickling crises and respiratory infections was not influenced. The initial favourable response was not, however, maintained; in 3 of the 4 cases the haemoglobin concentration fell to the pre-treatment level after 2 months' treatment and there was no further response even when the dosage was raised to the point of nausea and vomiting. In 3 of the 4 patients there was laboratory evidence of hypothyroidism within a few weeks with a dosage of 2 to 3 mg. per kg. daily. Goitre developed in all 3 after 7 months' treatment and myxoedema as well in one. In 2 of these patients biopsy of the thyroid gland revealed extreme hyperplasia. When the drug was withdrawn all evidence of hypothyroidism disappeared.

The authors consider that the failure of cobalt to maintain the initial haematopoietic response was due either to the developing hypothyroidism or to another, different, toxic action, and that cobalt should not be indiscriminately combined with other haematinic preparations because of the danger of hypothyroidism, especially in pregnancy and the iron-deficiency states.

A. J. Duggan

744. **Renal Hemodynamic Studies in Adults with Sickle Cell Anemia**
J. N. ETTELDORF, J. D. SMITH, A. H. TUTTLE, and L. W. DIGGS. *American Journal of Medicine* [*Amer. J. Med.*] **18**, 243–248, Feb., 1955. 6 figs., 8 refs.

At the John Gaston Hospital, Memphis, Tennessee, renal function was studied in 10 patients aged 16 to 37 suffering from established sickle-cell anaemia. At the time the renal function tests were carried out haematuria was not present in any of the patients. In order to demonstrate the relationship, in patients with sickle-cell anaemia, of age to renal function the authors include in composite tables and figures the results previously obtained in a group of children aged 4 to 11 years (*Amer. J. Dis. Child.*, 1952, **83**, 185). It was found that renal function was eventually impaired with increasing age. The glomerular filtration rate, effective renal blood and plasma flow, and tubular excretory capacity for *para*-aminohippurate remained normal or above normal until the age of 20. Between 20 and 30 years of age the glomerular filtration rate decreased markedly, and after the age of 30 all functions were seriously affected. The authors state that the pathological changes in the kidney in sickle-cell anaemia have not been adequately studied, but that a review of necropsy reports indicates progressive changes with age, which might explain the deterioration of renal function in the adult. *G. W. Csonka*

745. **The Influence of the Vagus Nerves on the Formation of the Intrinsic Anti-anaemic Factor.** (Влияние блуждающих нервов на формирование внутреннего начала антианемического фактора)
V. A. SAMTSOV. *Архив Патологии* [*Arkh. Patol.*] **17**, 22–28, Jan.–March, 1955. 19 refs.

The author suggests that the production of Castle's intrinsic factor is subject to nervous regulation. Reticulocytes were counted in rabbits before and after the subcutaneous injection of neutralized gastric juice from dogs, some of which had previously been given atropine while others had undergone vagotomy. While gastric juice from normal dogs caused a rise in the reticulocyte

count, no such response occurred with juice from the dogs given atropine or from the vagotomized dogs. Reticulocyte counts carried out on 3 patients with peptic ulcer before and during the administration of atropine confirmed this observation, there being a significant fall in the reticulocyte count after giving atropine.

L. Crome

NEOPLASTIC DISEASES

746. Intracellular Protein Resembling Russell Bodies in Malignant Lymphomas Associated with Acquired Hemolytic Anemia

H. RAPPAPORT and F. B. JOHNSON. *Blood* [*Blood*] **10**, 132–144, Feb., 1955. 10 figs., 32 refs.

The anaemia commonly found in the primary reticuloses is often haemolytic, and in some cases immune auto-antibodies have been demonstrated. The site of production of these antibodies is unknown, but it has been suggested that they may arise in the proliferating abnormal tissue. This paper from the U.S. Armed Forces Institute of Pathology and Veterans Administration Central Laboratory for Anatomical Pathology describes the occurrence, in neoplastic lymphocytes and macrophages from 3 patients with haemolytic anaemia associated with reticuloses, of material resembling Russell bodies, which are granular or hyaline inclusions with acidophil staining properties sometimes found in plasma cells. The first patient was suffering from chronic lymphatic leukaemia, and the other 2 from a form of reticulosis described by the authors as " malignant lymphoma ", of lymphocytic type in one case and of follicular type in the other. Large amounts of intracellular protein were found which resembled Russell bodies both in appearance and in histochemical reaction; it was present both in neoplastic lymphocytes and in non-neoplastic macrophages, and was Schiff-positive.

The authors discuss their observations in relation to abnormal protein production in malignant lymphomata in general and to the production of the auto-antibodies responsible for the accompanying haemolytic anaemia in particular. They suggest that this intracellular material may be the cytological manifestation of the production by the neoplastic cells of malignant lymphomata of abnormal proteins which " may play an important part in the immunological mechanisms responsible for the development of acquired hemolytic anemia in association with malignant lymphomas ".

A. S. Douglas

747. Hepatic Fibrosis in Children with Acute Leukemia after Therapy with Folic Acid Antagonists

J. COLSKY, E. M. GREENSPAN, and T. N. WARREN. *Archives of Pathology* [*Arch. Path.* (*Chicago*)] **59**, 198–206, Feb., 1955. 6 figs., 19 refs.

In 5 out of 7 children with acute leukaemia treated with the folic acid antagonists amethopterin and aminopterin a clinical remission of variable degree was obtained, but evidence of hepatic insufficiency appeared. All 5 ultimately died and 3 came to necropsy. In these cases the liver showed an increase in periportal fibrous tissue, with proliferation of the bile ducts and capillary blood vessels. In all of them there was some evidence of fatty degeneration, and in one there was considerable central necrosis of the lobules. No such changes were observed in the liver in a series of 50 adult patients who had received prolonged treatment with large doses of folic acid antagonists.

The aetiology of the hepatic fibrosis in these cases is discussed, but no firm conclusion can be drawn from the information available. It is suggested that the removal of infiltrating leukaemic cells by treatment may result in a tissue reaction with local scar formation, or that folic acid antagonists, by interfering with the metabolism of choline, betaine, and methionine, may cause a nutritional deficiency state predisposing to fibrosis. Another possible factor, in view of the occurrence of these fibrotic changes only in children, is a greater sensitivity of young organs to metabolic antagonists of essential nutrients.

Mary D. Smith

748. Myleran in Chronic Myeloid Leukaemia

D. A. G. GALTON and M. TILL. *Lancet* [*Lancet*] **1**, 425–430, Feb. 26, 1955. 5 figs., 11 refs.

The authors, working at the Chester Beatty Research Institute, London, report the results obtained with " myleran " (1 : 4-dimethane sulphonyloxybutane) in the treatment of 31 patients suffering from chronic myeloid leukaemia. Administration of myleran was the sole therapeutic measure in 12 cases, while in 19 radiotherapy (including the use of radioactive phosphorus) and drugs other than myleran had already been tried. Myleran was taken by mouth in tablets containing 0·5 mg. and 2 mg. At first a short intensive course of 100 to 150 mg. in 1 to 6 days was given, but because of severe bone-marrow depression this form of treatment was abandoned and a standard dosage of 0·06 mg. per kg. body weight daily was administered for 3 to 7 months, the total dose being regulated by the clinical and haematological response. Subsequent treatment was deferred until symptoms returned, as they invariably did 5 to 18 months later. Remissions after a second and third course of myleran were usually shorter and did not exceed one year in duration.

In an attempt to prevent further relapses 6 patients were treated continuously, the leucocyte count being reduced to 10,000 to 20,000 per c.mm. and maintained there with appropriate doses of myleran; 11 patients who had not received myleran previously were similarly treated. The dosage required for this form of maintenance therapy varied from 0·5 mg. to 6 mg. daily, but after only 23 months 3 patients developed resistance to the drug. Of 11 patients treated with myleran alone, 7 were still alive but only 2 had been observed for more than 3 years from the time of diagnosis.

The authors conclude that until further evidence is available radiotherapy is the treatment of choice in chronic myeloid leukaemia, but that myleran is a suitable substitute when radiation is either not available or contraindicated. Myleran is also valuable in those cases in which response to radiation has been unsatisfactory. It causes few side-effects.

D. G. Adamson

Respiratory System

749. **Prediction of Maximum Breathing Capacity from Timed Vital Capacity**
C. D. NEEDHAM, M. C. ROGAN, and I. MCDONALD. *British Journal of Tuberculosis and Diseases of the Chest* [*Brit. J. Tuberc.*] **49**, 30–37, Jan., 1955. 4 figs., 5 refs.

The maximum breathing capacity (M.B.C.) and timed vital capacity (T.V.C.) were measured at the Aberdeen General Hospitals in 623 subjects, 305 of whom were suffering from various cardiac or respiratory diseases. For the T.V.C. the unusually long period of 2 seconds was used, enabling it to be measured on an ordinary spirometer. A linear relation was shown to exist between the M.B.C. and the 2-minute T.V.C., and it is concluded that the former can be predicted with reasonable accuracy from the latter by means of regression equations. The equation calculated from the data for all subjects grouped together is: M.B.C. (in litres per minute)$=3{\cdot}7+28{\cdot}6\times$T.V.C. (in litres). Other regression equations are given for subjects in various age and sex categories. Patients with ankylosing spondylitis were excluded from the present study because their M.B.C. : T.V.C. ratio was very much higher than in any other group of patients. *W. A. Briscoe*

750. **Bronchial Carcinoma. Survey of 317 Patients**
J. R. BIGNALL. *Lancet* [*Lancet*] **1**, 786–790, April 16, 1955. 7 refs.

A survey is presented of 317 cases of bronchial carcinoma seen at the Brompton and Royal Marsden Hospitals, London, during 1951 and followed up for one year. Since the Brompton Hospital deals only with diseases of the chest and the Royal Marsden is a cancer hospital the patients were to a large extent selected. The diagnosis was based on histological evidence at thoracotomy or necropsy, clinical or radiological evidence of metastases, and suggestive appearances on bronchoscopy. In only 2·5% of patients did the diagnosis rest purely on clinical and radiological evidence of pulmonary abnormalities. The series included a high proportion of patients between 50 and 60 years of age and an unexpectedly small number of women over 70 years. The difficulty of determining the true frequency of the main histological types is discussed. The author points out that the classification of a tumour depends on the particular portion examined, and may have to be altered when the whole tumour is examined and the findings compared with those at biopsy. On the whole there were fewer undifferentiated tumours in this series than is usually the case.

About half the patients had had signs and symptoms for more than 2 but less than 4 months before admission to hospital. It is pointed out that the duration of symptoms does not indicate the age of the tumour and the fact that the disease is in an advanced stage does not necessarily mean that the patient has been ill for long. A lung cancer has to be well advanced to give rise to radiological shadows, and the author cites Boucot and Sokoloff (*Amer Rev. Tuberc.*, 1954, **69**, 164; *Abstracts of World Medicine*, 1954, **16**, 44), who found that of a group of patients whose disease was discovered by mass radiography, the proportion in whom the growth could be resected was no higher in those without symptoms than in those with symptoms.

Thoracotomy was performed in 25% of the cases, but resection was possible in only 18%. Of the total number of patients, 77 were alive 2 years after the onset and in 31 of these the tumour had been removed. If the tumour was not removed few patients survived 2 years from the time of diagnosis. Of 120 patients not considered suitable for surgery, 36 received "radical" radiotherapy (more than 4,000 r tumour dose) and 84 palliative radiotherapy (less than 4,000 r); of the former group, 19 survived for one and 9 for 2 years; of the latter group, 19 lived a year and only one was alive after 2 years.

The author discusses the pattern of the mode of death in these cases [hitherto a neglected aspect]. In view of the poor outlook it would certainly seem worth while, as he suggests, to inquire whether more cannot be done to relieve the suffering and ease the manner of dying of patients with bronchial carcinoma.

Ronald S. McNeill

See also Tuberculosis, Abstract 680.

751. **Clinical Experience with Pneumoperitoneum in the Treatment of So-called Hypertrophic Emphysema**
A. L. BANYAI and L. H. HIRSH. *Diseases of the Chest* [*Dis. Chest*] **27**, 121–127, Feb., 1955. 4 refs.

The authors advocate induction of pneumoperitoneum in the treatment of pulmonary emphysema, the object being to restore the function of the diaphragm and thereby improve pulmonary ventilation. In their experience the most satisfactory procedure is to introduce 50 ml. of air at a time to a total of 500 to 600 ml. in the initial treatment, and to give refills of this total amount at weekly intervals. The patient is encouraged to wear an abdominal support in order to limit the amount of air required. The authors state that while the duration of therapeutic pneumoperitoneum must depend on each patient's needs, they have continued it in some cases for years. Aminophylline, antispasmodic agents, and antibiotics are given, and digitalis is administered if there is heart failure. The authors claim that this is the most effective method of treating pulmonary emphysema. [Details of cases thus treated are not given.]

K. C. Robinson

752. **Pleural Effusion. A Statistical Study of 436 Patients**
E. C. LEUALLEN and D. T. CARR. *New England Journal of Medicine* [*New Engl. J. Med.*] **252**, 79–83, Jan. 20, 1955. 7 refs.

Urogenital System

753. **Effect of Adrenocorticotropic Hormone (ACTH) and Cortisone on Proteinuria and Hematuria in the Nephrotic Syndrome**

W. HEYMANN, C. GILKEY, and M. SALEHAR. *Pediatrics* [*Pediatrics*] **15**, 49–53, Jan., 1955. 3 figs., 11 refs.

From observations made on 15 children with nephrosis treated at the Western Reserve University Hospitals, Cleveland, Ohio, the effect of ACTH (corticotrophin) and cortisone in inducing diuresis and diminishing proteinuria seems to be due to the restoration of normal glomerular permeability for plasma proteins. This conclusion is based on the findings that a diminution in proteinuria preceded the onset of diuresis, that the time-lag between the decrease in proteinuria and the onset of diuresis was related to the degree of hypoproteinaemia, and that no marked decrease in proteinuria occurred in those cases in which a good diuresis did not occur.

L. H. Worth

754. **Prolonged Intermittent ACTH and Cortisone Therapy in the Nephrotic Syndrome; Immunologic Basis and Results**

K. LANGE, L. SLOBODY, and R. STRANG. *Pediatrics* [*Pediatrics*] **15**, 156–168, Feb., 1955. 5 figs., 27 refs.

The authors describe a study carried out at Flower and Fifth Avenue Hospitals, New York, which was designed to elucidate the immunological mechanism of the nephrotic syndrome as well as the mode of action of ACTH and cortisone in this condition. The senior author had previously demonstrated the presence of antibodies to human kidney tissue in the recovery stage of acute glomerulonephritis and during remissions of the nephrotic syndrome, although in the acute phase of these diseases they were usually absent. It was thought that these antibodies were probably present but were absorbed in the kidney during the acute stage. As the antigen–antibody reaction is a complement-binding one the serum complement levels in 69 of these patients were investigated, the normal range being first established by examination of 166 control subjects.

In 40 cases of acute and subacute glomerulonephritis the serum complement level was always low, and in 27 of 29 patients with the nephrotic syndrome the level was also low. It was observed that the level of complement rose before a spontaneous remission and fell before a relapse, these changes being independent of variations in plasma protein content. The low complement levels were not due to loss by urinary excretion, since comparable amounts were found in the urine of patients with proteinuria due to conditions such as the Kimmelstiel–Wilson syndrome or renal amyloidosis, in which the serum complement levels were found to be normal. In the cases of nephrotic syndrome large doses of ACTH or cortisone led to a rise in the complement level followed by diuresis, while relapses were preceded by a fall in this level. It is suggested that ACTH and cortisone may act by depressing antibody production. Both ACTH and cortisone given in high dosage for prolonged periods produced remissions in the majority of patients, and none of the 29 patients died during the observation period of 3 to 40 months. Relapses never occurred while maintenance doses of the steroids were being given. When last examined all but one of the patients were free from oedema.

G. W. Csonka

755. **Furadantin in Urinary-tract Infections. Clinical and Laboratory Studies**

H. M. TRAFTON, E. H. BEUTNER, J. J. PETRONIO, H. E. LIND, and M. CORREIA-BRANCO. *New England Journal of Medicine* [*New Engl. J. Med.*] **252**, 383–387, March 10, 1955. 11 refs.

This paper from Brooks Hospital, Brookline, Massachusetts, reports a clinical trial of the nitrofuran derivative "furadantin" (nitrofurantoin, *N.N.R.*) in the treatment of 49 cases of urinary infection (in 45 patients), most of which had failed to respond to antibiotics or other chemotherapeutic agents. The drug was given in doses of 300 to 800 mg. daily for 7 to 10 days and the cases were followed up for a minimum of 3 months with repeated microscopical and cultural examination of the urine.

Of 13 cases of acute, subacute, or postoperative infection, 6 were cured and 6 were markedly improved without relapse. However, the authors advise caution in the interpretation of the results in this group, because such infections may undergo spontaneous cure. Symptomatic improvement, often within 24 hours, occurred in 30 out of 36 cases of chronic infection; in 22 cases in this group the infecting organism disappeared as a result of treatment, but in 12 of them infection with the same or another organism recurred later. In only one case of chronic infection was there an apparent cure. *Pseudomonas aeruginosa* was unaffected by treatment with furadantin, this organism being present in 4 of the 7 cases in which there was no clinical response to therapy. On the other hand at least half of the infections with *Escherichia coli*, *Aerobacter aerogenes*, *Proteus* spp., *Streptococcus faecalis*, and *Micrococcus* spp. were cleared up permanently.

Altogether 60 patients received furadantin for urinary infection, of whom 15 reported reactions during the first course of therapy, 9 being able to continue treatment with the same or a reduced dose. Most of the reactions were mild gastro-intestinal disturbances, but fever, urticaria, and angioneurotic oedema were also noted. Although the sexes were equally represented in the group of 60 patients, 11 of the 15 suffering from reactions and 4 of the 6 whose treatment had to be stopped were women. Of 11 patients who received a second course, 4 demonstrated a diminished tolerance to the drug.

Charles Rolland

Endocrinology

756. Fluorohydrocortisone and Chlorohydrocortisone, Highly Potent Derivatives of Compound F

A. L. GOLDFIEN, J. C. LAIDLAW, N. A. HAYDAR, A. E. RENOLD, and G. W. THORN. *New England Journal of Medicine* [*New Engl. J. Med.*] **252**, 415–421, March 17, 1955. 11 figs., 7 refs.

It has been shown that 9-α-chlorohydrocortisone and 9-α-fluorohydrocortisone have both glucocorticoid and mineralocorticoid activity. The present paper from the Peter Bent Brigham Hospital, Boston, reports a comparative study of the metabolic and therapeutic effects of these two compounds. Chemical determinations and eosinophil counts were carried out by standard methods.

Preliminary tests on a patient with Addison's disease showed that the chloro- and fluoro- derivatives had a considerably more potent action than either cortisone or hydrocortisone (Compound F) in respect of both their glycogenic and sodium-retaining effects, and produced a greater and more prolonged eosinopenia. In a metabolic experiment on a patient with Addison's disease who was maintained on a constant diet, 3 mg. of chlorohydrocortisone and 0·25 mg. of fluorohydrocortisone were found to be equivalent to 1 mg. of deoxycortone. In another, similar patient fluorohydrocortisone was found to be as potent in sodium-retaining properties as aldosterone and to have a more prolonged action; a similar observation was made in a subject with normal adrenal function.

Clinically, patients with Addison's disease could be maintained satisfactorily on comparatively small doses of fluorohydrocortisone given by mouth (in the ratio of approximately 1 mg. of the fluoro- compound to 20 mg. of cortisone or hydrocortisone). On these small doses no 17-hydroxycorticoids could be detected in the urine by the Porter–Silber reaction. Thus effective substitution therapy with adrenal hormones can be continued during the administration of ACTH for the diagnostic evaluation of adrenocortical function. The authors conclude that satisfactory inhibition of the adrenal cortex can be achieved in normal subjects, and in female patients with the adrenogenital syndrome, by the oral administration of 1 to 2 mg. of fluorohydrocortisone per day.

Nancy Gough

757. Further Studies on the Nature of the Exophthalmos-producing Principles in Pituitary Extracts

G. K. SMELSER and V. OZANICS. *American Journal of Ophthalmology* [*Amer. J. Ophthal.*] **39**, 146–155, Feb., 1955. 4 figs., 17 refs.

Recent experimental work has suggested that the production of exophthalmos may be due to a hormone contained in anterior pituitary extracts acting in conjunction with a potentiating agent which is probably ACTH. At Columbia University College of Physicians and Surgeons, New York, experiments were carried out on young female guinea-pigs in an attempt to identify these substances. Ten days after thyroidectomy the animals were given daily for 12 days subcutaneous injections of various hormone preparations, including anterior pituitary extract and ACTH. They were killed the following day and the measurement from the supra-orbital notch to the limbus was determined in order to indicate the degree of exophthalmos. The orbital contents were also dissected, the fat, muscles, and glands weighed separately, and the amount of oedematous infiltration of the fat noted.

It was shown that exophthalmos, with hypertrophy of the orbital contents, was produced by combined injections of ACTH and standard beef pituitary extract, but not when either substance was given alone. The effect was enhanced when a more highly purified ACTH preparation was used, indicating that ACTH is the potentiating agent. It is suggested that the effect of ACTH is to stimulate the production of adrenocortical steroids which, acting synergistically with the pituitary extract, produce exophthalmos. This view is supported by the fact that when cortisone, as an example of such a steroid, was substituted for ACTH in the combined injection exophthalmos resulted, its degree being proportional to the dose of cortisone used.

In a further series of experiments relatively pure preparations of pituitary growth hormone, prolactin, and gonadotrophin, when injected separately with cortisone, failed to produce exophthalmos, but when relatively pure thyrotrophic hormone was injected along with cortisone, exophthalmos and typical orbital changes were readily produced. However, since the combined injection of several purified anterior pituitary hormones containing only traces of thyrotrophic hormone was more effective than equal quantities of purified thyrotrophic hormone, it is postulated that some other, as yet unknown, exophthalmogenic factor, additional to thyrotrophic hormone, must be present in the secretion of the anterior pituitary gland.

E. Lyons

758. Studies in Surgical Endocrinology. 1. The Urinary Excretion of 17-Hydroxycorticoids, and Associated Metabolic Changes, in Cases of Soft Tissue Trauma of Varying Severity and in Bone Trauma

F. D. MOORE, R. W. STEENBURG, M. R. BALL, G. M. WILSON, and J. A. MYRDEN. *Annals of Surgery* [*Ann. Surg.*] **141**, 145–174, Feb., 1955. 18 figs., bibliography.

This paper reports the results of investigation of the urinary excretion of 17-ketosteroids and 17-hydroxycorticoids in relation to clinical and metabolic events in 11 patients undergoing various types of surgical operation at the Peter Bent Brigham Hospital (Harvard Medical School), Boston. Nitrogen, potassium, sodium, and, in some instances, chloride balances were performed, and total body water and total exchangeable sodium and

potassium were determined. Similar studies were carried out on a control group of normal subjects of constant weight, the changes produced by a period of starvation being also noted, since post-traumatic changes are frequently contrasted with those of starvation.

In 3 cases of appendicectomy, including one in which there had been a ruptured appendix with subsequent pelvic abscess, the changes in 17-ketosteroid excretion were insignificant, but excretion of 17-hydroxycorticoids increased after operation as the eosinophil count fell; in the septic case this was maintained until the abscess was drained, being paralleled by high nitrogen loss and a prolonged catabolic phase, with loss of 12% of body weight.

In 5 cases of soft-tissue trauma there was, in general, fair correlation between clinical severity, nitrogen loss, the fall in the eosinophil count, and the rise in 17-hydroxycorticoid excretion, but 17-ketosteroid excretion could not be related to the other events. In 2 cases the characteristic pattern of 17-hydroxycorticoid excretion was distorted; the first, a case of second-degree burns, showed an unexpectedly low hormone output for the first few days, and in the second, a case of cancer of the breast, the rise in hormone output was prolonged in spite of the fact that the postoperative eosinophil count showed the normal changes.

Finally, in 3 cases of trauma of bone there was a consistent tendency to an inverse correlation between 17-hydroxycorticoid excretion and the eosinophil count. Case histories and detailed charts are presented for all the cases discussed. *Nancy Gough*

THYROID GLAND

759. **Clinical Value of the TSH Test in the Diagnosis of Thyroid Diseases**
G. A. BISHOPRIC, N. H. GARRETT, and W. M. NICHOLSON. *American Journal of Medicine* [*Amer. J. Med.*] **18**, 15–19, Jan., 1955. 6 refs.

In the study here reported from Duke University and Hospital, Durham, North Carolina, an attempt was made to establish the reliability of measuring the uptake of radioactive iodine (^{131}I) by the thyroid gland after stimulation by thyroid stimulating hormone (T.S.H.) as a means of differentiating primary from secondary hypothyroidism. Of the 34 subjects studied, 12 had primary hypothyroidism and in 6 it was secondary to hypopituitarism; the other 16 were normal subjects, 10 of whom took varying amounts of thyroid extract experimentally and 2 had received iodine inadvertently just before the experiment began. Tracer doses of 10 to 20 μc. of ^{131}I were given and the thyroid uptake at 3 and at 24 hours was measured both before and after the administration of T.S.H.

In normal subjects there was a mean increase of 19·8% in the 3-hour uptake of ^{131}I and of 34·5% in the 24-hour uptake. In 5 of the patients with untreated primary hypothyroidism the result was a fall of 2·4% in the 3-hour uptake but this was reduced to 1·6% at 24 hours; similar results were obtained in patients with treated primary hypothyroidism. Of the 6 patients with secondary hypothyroidism, 5 responded to T.S.H., the results for all 6 showing a mean increase in uptake of 7·3% at 3 hours and 19·7% at 24 hours. The authors conclude that by this method primary hypothyroidism can be differentiated from euthyroidism and point out that 5 of the 6 cases of secondary hypothyroidism were differentiated from primary hypothyroidism. *C. L. Cope*

760. **Carcinoma and Thyroid Nodules. The Problem in an Endemic Goiter Area**
J. M. MILLER. *New England Journal of Medicine* [*New Engl. J. Med.*] **252**, 247–251, Feb. 17, 1955. 20 refs.

The clinical records of 600 female patients admitted to the wards or attending a clinic at the Henry Ford Hospital, Detroit, during the years 1943 to 1952 inclusive were examined, the object being to determine the incidence of goitre, the frequency with which thyroid cancer was diagnosed by biopsy or was an unexpected finding at operation, and the mortality from cancer of the thyroid gland.

A total of 68 patients, 46 from an area of endemic goitre, had nodules in the thyroid, the size of the nodules being 1 to 2 cm. in 40 and 2 to 5 cm. in 28. During the 10-year period thyroidectomy was performed for nontoxic goitre in 435 cases and in 16 of these thyroid cancer, previously unsuspected, was found, an incidence of 3·7%; when the figures for " estimated nodular glands seen and unsuspected carcinomas found " were combined the incidence was 0·2%. The author states that there was one case of unsuspected cancer in about every 250 cases of toxic nodular goitre subjected to operation.

During the period under review 32 new cases of cancer of the thyroid were seen, representing 0·7% of all cases of cancer admitted to the hospital. In 17 of these malignancy was unsuspected; all 17 patients were alive in 1953. There were only 8 deaths from cancer of the thyroid in the 10-year period. *D. G. Adamson*

761. **Variations in the Response of Individuals of Different Ages to an Antithyroid Compound (Methimazole)**
T. H. MCGAVACK, J. CHEVALLEY, and S. PEARSON. *Journal of the American Geriatrics Society* [*J. Amer. Geriat. Soc.*] **3**, 96–105, Feb., 1955. 3 figs., 34 refs.

At the Metropolitan Hospital (New York Medical College), Welfare Island, New York, the effect of age on the response to the antithyroid agent methimazole (propylthiouracil) was studied in 175 patients with hyperthyroidism who were divided into three age groups: (I) 15 to 34 years, (II) 35 to 54 years, and (III) 55 to 83 years. When a daily dose of 30 to 40 mg. was given it appeared that Group I responded most quickly, but signs of improvement appeared in all groups within 2 weeks, and no significant differences were seen between them in the time taken to bring the hyperthyroidism under control, in the biochemical findings, or in objective clinical observations such as weight gain; however, the pulse rate returned to normal more frequently in Group I. The groups did not differ significantly in respect of change in size of the gland, or in the incidence of " cure " [the criteria of which are not discussed].

[The frequency with which a large proportion of the total number of subjects had to be excluded from the analyses because certain essential data were not available, or for some unspecified reason, casts doubt on the value of these observations as a whole.] *J. N. Agate*

762. **Carbimazole in Thyrotoxicosis**
K. KIRKEBY and O. RØMCKE. *Lancet* [*Lancet*] **1**, 374–376, Feb. 19, 1955. 1 fig., 11 refs.

The antithyroid action of carbimazole is presumed to be the result of hydrolysis, with gradual release of a compound identical with methimazole; unlike most other antithyroid drugs carbimazole is tasteless. In this paper from Drammen Hospital, Drammen, Norway, the results obtained with carbimazole in the treatment of 56 patients with thyrotoxicosis are reported. It was found that with a dosage of 30 to 50 mg. daily the basal metabolic rate fell to normal in 3 to 6 weeks. General side-effects were noted in only one patient, the drug having to be discontinued because of a rash. The authors note, as others have done, that the incidence of side-effects is less with carbimazole than with methimazole. Moreover, goitrogenic reactions were less frequently encountered in this series of patients than in patients given methylthiouracil or propylthiouracil. *G. S. Crockett*

ADRENAL GLANDS

763. **Use of ACTH in the Diagnosis of Adrenal Cortical Insufficiency**
D. JENKINS, P. H. RORSHAM, J. C. LAIDLAW, W. J. REDDY, and G. W. THORN. *American Journal of Medicine* [*Amer. J. Med.*] **18**, 3–14, Jan., 1955. 6 figs., 34 refs.

In this report from Harvard Medical School the authors summarize 7 years' experience in the clinical use of ACTH (corticotrophin) for the diagnosis of adrenocortical insufficiency. Up to 1950 ACTH preparations were impure, but later they were purified by differential elution from oxycellulose columns. Two types of ACTH test are discussed—the rapid and the intravenous tests. In the rapid ACTH test the percentage fall in the number of eosinophil granulocytes is observed 4 hours after a single intramuscular injection of 25 mg. of ACTH. A review of the results of 545 tests showed that the decrease in the number of circulating eosinophils was less than the arbitrary norm of 50% in 24% of the control group (104 cases). The 95% "confidence limits" of the two groups showed extensive overlap, but this overlap was much reduced by using modern purified preparations of ACTH, with which the mean fall in normal subjects was 63%, in patients with Addison's disease 7%, and in those with hypopituitarism 24%. The rapid test has a limited value as a screening procedure.

In the intravenous ACTH test, which aims at maximal adrenal stimulation, 25 mg. of ACTH in 500 ml. of normal saline is infused intravenously over 8 hours. The mean eosinophil count in the control group fell by 94%, but in patients with Addison's disease by only 1%; thus the two groups were clearly distinguished, there being no overlap. After such stimulation the increase in 17-ketosteroid excretion was more irregular and showed considerable overlap between the two groups. The rise in output of 17-hydroxycorticoids may also be variable, but nevertheless showed only slight overlap in the 95% confidence limits. Repetition of the intravenous ACTH stimulation test on successive days will accentuate the difference in ambiguous cases, particularly in those in which adrenocortical atrophy is secondary to hypopituitarism. The use of ACTH in a gelatin vehicle—2 doses of 40 units intramuscularly at a 12-hour interval—gave similar results to those of the intravenous ACTH test.

The authors regard the measurement of 17-hydroxycorticoid excretion as the index of choice in evaluating the effect of adrenocortical stimulation. They emphasize that adrenaline should not be used for this test. Only 6 cases of serious reaction to intravenous ACTH have occurred, all in subjects with adrenal insufficiency. This may take the form either of an immediate anaphylactoid reaction, which can be controlled by administration of adrenaline, or of a delayed reaction, manifested by fever and malaise after several hours. *C. L. Cope*

764. **Adrenocortical Capacity and the Metabolism of Cortisol in Elderly Patients**
F. H. TYLER, K. EIK-NES, A. A. SANDBERG, A. A. FLORENTIN, and L. T. SAMUELS. *Journal of the American Geriatrics Society* [*J. Amer. Geriat. Soc.*] **3**, 79–84, Feb., 1955. 2 figs., 7 refs.

The urinary 17-ketosteroid excretion of elderly patients is less than that of young adults, and it has been suggested that this is because adrenal cortical function diminishes with increasing age. The authors, working at the University of Utah College of Medicine, Salt Lake City, have estimated the 17-hydroxycorticosteroid content of the plasma of patients aged 66 to 92 years, excluding any with acute inflammatory or endocrine disorders. The mean morning plasma 17-hydroxycorticosteroid level in a number of these patients was higher than in a group of young adults [the size of which is not stated], but the difference was not statistically significant. After an infusion of ACTH (corticotrophin), however, the mean level was significantly higher in 5 of the older subjects than in a larger group of young adults. Similarly, after the infusion of 1 mg. of hydrocortisone per kg. body weight the level of 17-hydroxycorticosteroids in the blood rose higher in the older group; however, the rate of removal of hydrocortisone from the blood was the same in both groups at first, though it fell off later in the older group.

The conclusion is drawn that there is no deficiency of secretion or metabolism of 17-hydroxycorticosteroids in the elderly, the differences observed between the blood levels of younger and older subjects in the various circumstances studied being explained as due to differences in the volume of distribution. These might be related to differences in body fat distribution, although no correlation between the effect of an infusion of hydrocortisone on the plasma level and the degree of obesity of the subject was observed. Whatever the explanation,

it might be expected that smaller therapeutic doses of ACTH and cortisone would be needed by elderly patients than by young adults. *J. N. Agate*

765. **Adrenocortical Function during Long-term Cortisone Therapy. Further Observations**
E. W. FREDELL, H. P. JOHNSON, M. A. KRUPP, E. P. ENGLEMAN, and A. K. MCGRATH. *Archives of Internal Medicine* [*Arch. intern. Med.*] **95**, 411–418, March, 1955. 3 figs., 18 refs.

At the Veterans Administration Hospital, San Francisco, adrenocortical function was assessed in 19 patients who had been receiving treatment with cortisone for periods of one to 4 years by determining the eosinophil count and the level of urinary 17-ketosteroid and urinary corticoid excretion after 5 consecutive days of intravenous infusion of ACTH (corticotrophin). Adrenocortical response was considered adequate if two of the following criteria were met: (1) a decrease of more than 60% in the number of eosinophil granulocytes; (2) an increase of more than 50% in urinary 17-ketosteroid excretion; and (3) an increase of more than 50% in urinary corticoid excretion.

The results, which are presented in several ways in tables and diagrams, showed that there was a slight tendency for a longer period of stimulation with corticotrophin to be necessary in order to evoke an adequate adrenal response when cortisone therapy had been prolonged. The authors conclude that the adrenal cortex which has been suppressed by the administration of cortisone is still responsive to stimulation with ACTH. It was noted that long-term cortisone therapy had no effect on thyroid function.

[Unfortunately the results are presented in a form which makes them difficult to assess.] *C. L. Cope*

766. **The Function of the Adrenal Cortex in Counteracting the Effect of Insulin.** (Die Funktion der Nebennierenrinde in der Insulingegenregulation)
R. FROESCH. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **85**, 121–127, Feb. 5, 1955. 4 figs., 40 refs.

It has been known for some time that hypoglycaemia induced by insulin causes an increased secretion of adrenaline into the blood from the adrenal medulla. The introduction by Nelson and Samuels (*J. clin. Endocrinol.*, 1952, **12**, 519) of a method for the quantitative assay of 17:21-hydroxycorticosteroids in the blood has now made possible the direct study of the effect of insulin hypoglycaemia on the adrenal cortex. A series of experiments were carried out at the University Polyclinic, Zürich, to determine whether insulin hypoglycaemia was accompanied by any change in the serum hydroxycorticosteroid level in normal subjects and patients with the adrenogenital syndrome—where the relation between the anterior pituitary gland and the adrenal cortex is disturbed and there is therefore no possibility of regulating the effect of insulin by means of an increased secretion of hydroxycorticosteroids. The results of these experiments [the details of which should be sought in the original paper] may be summarized as follows.

(1) Insulin hypoglycaemia produces an initial transient fall in the level of 17:21-hydroxycorticosteroids in the blood, followed by a rise with increased urinary excretion. The increased secretion of hormones was shown to be due to the hypoglycaemia itself, and not to a direct effect of insulin. (2) The extent of the adrenal cortical response is determined mainly by (*a*) the duration and degree of the hypoglycaemia and (*b*) by the condition and responsiveness of the adrenal cortex, which seem to be subject to great variation in the course of the day. (3) The stimulation by insulin hypoglycaemia of the adrenal cortex seems to be mediated through ACTH (corticotrophin). (4) In 2 patients with congenital and one with acquired adrenogenital syndrome insulin hypoglycaemia was not regularly followed by an increase in the blood corticoid level. The blood sugar curves in insulin tolerance tests, however, were normal. (5) The hypoglycaemic effect of insulin is normally counteracted by the secretion by the adrenal glands of glucocorticoids and of another, more rapidly effective, agent which is probably adrenaline.

[This paper is worthy of careful study.]
V. C. Medvei

767. **Studies of Adrenal Function in Combat and Wounded Soldiers. A Study in the Korean Theatre**
J. M. HOWARD, J. M. OLNEY, J. P. FRAWLEY, R. E. PETERSON, L. H. SMITH, J. H. DAVIS, S. GUERRA; and W. H. DIBRELL. *Annals of Surgery* [*Ann. Surg.*] **141**, 314–320, March, 1955. 7 figs., 8 refs.

The effect on adrenal function of the chronic stress of front-line conditions was studied among U.S. troops in Korea. Eosinophil counts were performed daily on 3 successive days on 11 soldiers in non-combat areas. "The results were distributed about a mean of 142 with a standard deviation of 67." [In giving the results of these investigations the authors usually fail to specify the volume of blood to which the eosinophil counts refer. It would appear, however, that the figures given represent the number of cells per cubic centimetre of blood.] In 3 successive 24-hour collections of urine from 4 healthy soldiers in non-combatant areas the excretion of 17-ketosteroids ranged from 9·9 to 21·9 mg. a day and that of corticosteroids (formaldehydogenic compounds) averaged 2·2 mg. a day.

The mean eosinophil count of 21 men leaving the battle area for 24 hours' rest was 87 per c.cm. (S.D. 40), whereas that of 17 men examined in the front line was 154 per c.cm. (S.D. 59). No change occurred in the eosinophil count of 3 men as a result of an uneventful combat patrol. The urinary 17-ketosteroid excretion of men in the front line varied from day to day, being normal on some days and definitely elevated on others. In one group of 15 men it was possible to show that corticosteroid excretion tended to vary with danger.

Eosinophil counts were performed on 64 men wounded in action on their admission to a forward hospital and at intervals for varying periods thereafter. In all except 2 with minor wounds the count fell below 100 per c.cm., almost reaching zero in most of them. The urinary concentrations of sodium and potassium were determined

in 31 seriously injured casualties on admission and hourly thereafter. Sodium conservation and potassium diuresis were indicated by the development of a Na : K ratio of less than 1 in 27 of the 31 patients during the first few hours after injury.

No evidence of adrenal insufficiency was found: indeed, the most striking finding was the magnitude of the adrenal response to the stress of combat. The response to acute danger appeared to be comparable to that to major physical trauma. *Norval Taylor*

DIABETES MELLITUS

768. **Low-fat Diet and Therapeutic Doses of Insulin in Diabetes Mellitus**
I. SINGH. *Lancet* [*Lancet*] **1**, 422–425, Feb. 26, 1955. 10 refs.

The author describes an investigation of the value of a low-fat diet in the treatment of 80 patients with insulin-sensitive diabetes. The diet contained 20 to 30 g. of fat, 120 to 150 g. of protein, and sufficient carbohydrate to give a diet of optimal caloric content for the individual. The initial insulin dosage was such as to counteract the glycosuria; when the urine had been sugar-free for 48 to 72 hours, the insulin dosage was progressively reduced. Of the 80 patients, 50 became sugar-free in 3 to 6 weeks and 8 in 18 weeks; no further insulin was required in these cases. The insulin requirement of 12 patients was reduced from 80 to 120 units per day to one of 20 to 40 units. Glucose tolerance was tested in a small group of the patients during treatment and was found to have increased markedly. Hypoglycaemia developed in one case. *F. W. Chattaway*

769. **Effect of Kimmelstiel–Wilson Syndrome on Insulin Requirements in Diabetes**
J. W. RUNYAN, D. HURWITZ, and S. L. ROBBINS. *New England Journal of Medicine* [*New Engl. J. Med.*] **252**, 388–391, March 10, 1955. 9 refs.

Having noticed Kimmelstiel–Wilson lesions in the kidneys of 2 out of 3 patients who died of diabetic acidosis, and changes in insulin requirements coincident with the development of the Kimmelstiel–Wilson syndrome in 5 other patients, the authors of this paper from the Boston City Hospital and Harvard Medical School reviewed the clinical and necropsy records of 375 diabetic patients who died in the years 1940–52. Kimmelstiel–Wilson lesions were found in the kidneys of 138 of these patients. For the purpose of the present study 106 patients who had had diabetes for at least 3 years and had taken insulin for a minimum of 8 months and for whom detailed clinical records were available were selected, there being 54 who had Kimmelstiel–Wilson renal lesions and 52 who had not. These two groups were comparable in respect of age at death, duration of diabetes, and general level of insulin requirements. In each case the insulin dosage during a basal period, which was taken to be the mid-point in the course of the diabetes, and during the preterminal period—the months just before the terminal admission—was recorded.

In both groups there was a decrease of 2 units in the average daily insulin requirement between the basal and preterminal periods. Of the patients with Kimmelstiel–Wilson lesions, insulin requirements increased in 27·8% and decreased in 40·7%, the corresponding figures for the group without Kimmelstiel–Wilson lesions being 25% and 37%. The authors conclude that there was no significant difference between the two groups in respect of changes in insulin requirements. Of 15 patients who required no insulin during the preterminal period, none had acidosis and none had clinical evidence of the Kimmelstiel–Wilson syndrome, though 5 had Kimmelstiel–Wilson lesions in the kidneys at necropsy. Of 37 patients with oedema, albuminuria, and hypertension, Kimmelstiel–Wilson lesions were demonstrated in 29, and in 59% of this group (21 patients, including 6 of those without Kimmelstiel–Wilson lesions) there was a decrease in insulin requirements in the preterminal period. In 5 cases in which detailed dietetic histories were available a marked decrease in food intake accompanied the advance of the clinical Kimmelstiel–Wilson syndrome. There were 24 episodes of acidosis in 14 patients with Kimmelstiel–Wilson lesions and 11 episodes in 9 patients without the lesions, but diabetic acidosis occurred in only one patient with the clinical Kimmelstiel–Wilson syndrome. There was no striking correlation between the severity of the Kimmelstiel–Wilson lesions and the changes in insulin requirements.

The authors conclude that there is no evidence that the presence of Kimmelstiel–Wilson lesions in the kidneys is necessarily associated with a decrease in the severity of the diabetes and an infrequent occurrence of acidosis, although an amelioration of the diabetes often, but not invariably, occurs in patients with the clinical Kimmelstiel–Wilson syndrome, among whom acidosis is rare. This may be attributed to an accompanying diminution in food intake. *Charles Rolland*

770. **Neuropathy in Diabetes Mellitus**
J. D. MATTHEWS. *Lancet* [*Lancet*] **1**, 474–476, March 5, 1955. 7 refs.

The incidence of neuropathy in 545 diabetic patients at the Royal Infirmary, Edinburgh, and its relation to the patient's age, duration and severity of the diabetes, and the presence or absence of vascular disease were studied. Neuropathy, as shown by changes in reflex activity, muscle weakness, hyperaesthesia, and loss of sensation to light touch, pinprick, and vibration, was found in 37%. The author's findings are given in several tables; briefly they show that neuropathy is most commonly found (1) in older diabetic patients, (2) when diabetes has been present for 10 years or more, (3) in diabetics who require insulin, and (4) in those with vascular disease. The most important single factor in the development of neuropathy is, however, poor control of the diabetes, neuropathy being found in 64% of 237 in whom control was inadequate. There is as yet no satisfactory explanation of the occurrence of neuropathy in diabetes, but the author suggests that it is probably due to the disordered metabolism.
G. S. Crockett

The Rheumatic Diseases

771. **Ocular Changes in Acute Systemic Lupus Erythematosus**

F. CLIFTON and C. H. GREER. *British Journal of Ophthalmology* [*Brit. J. Ophthal.*] **39**, 1–10, Jan., 1955. 4 figs., 16 refs.

According to the authors the only report in the British literature of the histological examination of the eye in acute systemic lupus erythematosus is that of Semon and Wolff (*Proc. roy. Soc. Med.*, 1933, **27**, 153), who found only mild choroiditis and subretinal exudation. In the present paper the clinical, ophthalmological, and pathological findings in 2 further cases seen at Bristol hospitals, both of which terminated fatally, are described. On general examination no new or unusual features were seen, but a notable finding on histological examination of the eye was the presence of cytoid bodies in the nerve fibre layers of the retina, particularly at the posterior pole and around the disk. The rods and cones near the disk had undergone granular degeneration, inducing a shallow retinal detachment. Differing views on the nature and origin of cytoid bodies and the conditions in which they occur are discussed. The authors suggest that cytoid bodies are exudates in the nerve fibre layer resulting from damage to the capillary endothelium which permits the escape of plasma and erythrocytes.

F. D. McAuley

ACUTE RHEUMATISM

772. **Treatment of Acute Rheumatic Fever in Children. A Co-operative Clinical Trial of A.C.T.H., Cortisone, and Aspirin**

MEDICAL RESEARCH COUNCIL and AMERICAN HEART ASSOCIATION. *British Medical Journal* [*Brit. med. J.*] 1, 555–574, March 5, 1955. 6 figs., 6 refs.

This report gives the detailed results of a large-scale, long-term investigation into the relative efficacy of ACTH (corticotrophin), cortisone, and aspirin in suppressing the manifestations of acute rheumatism and in preventing rheumatic heart disease. Centres on both sides of the Atlantic collaborated in the investigation, which was planned jointly by the Rheumatic Fever Working Party of the Medical Research Council of Great Britain and the Council on Rheumatic Fever and Congenital Heart Disease of the American Heart Association.

In all, 497 children under 16 were treated, most of them for a standard period of 6 weeks, and were observed in hospital for a further 3 weeks after the completion of treatment. After discharge, follow-up examinations were made at specified intervals up to one year from the start of treatment. All patients were protected against streptococcal infection with penicillin and sulphadiazine while in hospital, and subsequent throat infections were treated with penicillin. The allocation of patients to the three treatment groups was made at random according to a predetermined order which was unknown to the admitting physician. The diagnostic criteria were laid down as precisely as possible. "Major" manifestations were carditis, polyarthritis, chorea, subcutaneous nodules, and erythema marginatum. Fever, raised erythrocyte sedimentation rate (E.S.R.), evidence of previous streptococcal infection, increased P–R interval, and a reliable history of rheumatic fever or evidence of pre-existing rheumatic heart disease were regarded as "minor" manifestations. The presence of 2 major or 1 major and 2 minor manifestations was required for diagnosis. The three treatment groups were approximately equal in size and largely similar with regard to the distribution of these manifestations in the two countries, except that nodules were more frequent in Great Britain. [For details of the dosage schedules employed, the reader should consult the original paper.]

The effects of treatment on the temperature and pulse rate were roughly the same in all 3 groups, though in those treated with hormones the pulse rate showed some tendency to rise during the 6th to 9th weeks. The E.S.R. fell more rapidly with hormone treatment, but by the 13th week it had reached the same level in all groups. No differences were discovered in the effect on joint involvement, chorea, and erythema marginatum. New nodules appeared during treatment in all groups, but persisted longer in the group receiving aspirin.

There was a tendency for patients treated with ACTH or cortisone to show a temporary increase in heart size, but the P–R interval, when prolonged, showed a more rapid initial decrease in these groups. The development of cardiac murmurs bore no relation to treatment. The disappearance of soft apical systolic and mid-diastolic murmurs was more rapid with hormone treatment, but there were no differences in their incidence at the end of a year. The appearance and disappearance of loud apical systolic and basal diastolic murmurs were unrelated to therapy and at the end of a year there was no difference between the groups in respect of this type of murmur. The occurrence and course of pericarditis were also unaffected by the type of treatment received, which similarly had no appreciable effect on the course of the disease in seriously ill patients with congestive heart failure.

Most of the patients receiving the hormones, but relatively few of those receiving aspirin, developed side-effects. Only 6 deaths occurred among the 497 patients.

It is concluded that there is no evidence to suggest that rheumatic fever in children can be uniformly arrested by any of the 3 agents used or that there is any significant difference between them in their effect on the cardiac status of the patient at the end of one year.

[This model investigation has produced a wealth of data to which no abstract can do full justice.]

G. Loewi

773. **Chemoprophylaxis of Acute Rheumatism in Children.** (Chemo-prophylaxis van acuut rheuma bij kinderen)
S. VAN CREVELD, M. G. STRONK, M. R. H. STOPPELMAN, and G. MAK. *Nederlandsch tijdschrift voor geneeskunde* [*Ned. T. Geneesk.*] **99**, 614–618, Feb. 26, 1955. 3 refs.

The main observations made in this report on a 6-year trial (1948–54) of sulphadiazine prophylaxis carried out in the out-patient clinics of the Children's Hospital of the University of Amsterdam on 172 out of 246 children with a history of acute rheumatism are: (1) a delay of 3 months after the acute attack is unnecessary, and prophylaxis can be instituted as soon as haemolytic streptococci have disappeared from the throat; (2) recurrences were more frequent when prophylaxis was irregular or interrupted; (3) of 2,476 bacteriological examinations of throat swabs, only 71 showed the presence of haemolytic streptococci, and 4 of 49 strains examined were resistant to 8 μg. of sulphadiazine per ml. or more; and (4) there were no serious side-effects resulting from prophylactic treatment with sulphadiazine. It is claimed that the relapse rate in acute rheumatism can be reduced by chemoprophylaxis.

R. Crawford

CHRONIC RHEUMATISM

774. **The Old Arthritic Family.** (La vieille famille arthritique)
M. G. GIRAUD. *Montpellier médical* (*Montpellier méd.*] **46**, 591–598, Dec., 1954.

The term " arthritis " has remained in general use in spite of attempts to replace it by more exact definitions. Similarly, the " arthritic family " is a concept well known to clinicians, both ancient and modern. The arthritic " soil " or constitutional predisposition may consist of several components, but some discrimination is here necessary. Thus simple obesity may be included, but not the glandular types; similarly, a hyperglycaemic tendency may be a significant feature of the arthritic diathesis, but not diabetes in young subjects or progressive or unstable diabetes. In those possessing the required constitution, the precipitation from the blood of certain substances will have characteristic effects. Gout is an example of such a condition, the sufferer being handicapped by his endogenous hyperuricaemia, though the precipitate consists not only of urates, but also of cholesterol and oxalates; deformities of the joints and the growth of tophi follow in due course. Nephrolithiasis has been called " the brother of gout ", because somewhat similar constitutional factors are present, although the clinical expression is directed towards a different system. Cholesterol precipitation results in gall-stones, xanthomata, and xanthelasma, and analogous processes are probably at work in the formation of salivary and pancreatic calculi and arterial atheroma.

It is possible, therefore, that a similar type of acute reaction to the precipitation of some metabolite may account for those chronic and degenerative forms of rheumatism to which the term " arthritic diathesis " is empirically applied, and the symptomatology of which includes the presence of peri- and intra-articular " deposits " and of " nodes " with accompanying tissue reactions. The characteristic sudden bursts of transient activity suggest an unstable and absorbable precipitate. It is here, possibly, that allergy and " stress " play their part.

David Preiskel

775. **Relief of Rheumatic Pains with Diethylamine Salicylate Cream: a Clinical Trial**
T. H. HOWELL. *British Journal of Physical Medicine* [*Brit. J. phys. Med.*] **18**, 62–63, March, 1955. 2 refs.

Diethylamine salicylate in a vanishing-cream base was tried at St. John's Hospital, Battersea, in the treatment of 24 patients suffering from soft-tissue pains associated with arthritis. The method of the trial was as follows. All the patients were given a dummy cream to apply to the painful areas daily for 4 weeks. A cream which was indistinguishable from this but which contained 10% diethylamine salicylate was then supplied for similar application. Assessment of the results from the patients' replies to careful questioning revealed that 6 obtained relief of pain with the dummy cream and 19 with the test cream. Similar results were obtained in two further trials in which the effect of the same test cream was compared with that of creams containing 1 in 5,000 adrenaline and 1% ephedrine hydrochloride respectively. [It is not stated whether the test cream was given during the first 4-week period in any experiment for comparison.]

The possible mode of action of the diethylamine salicylate cream is discussed. The author suggests that the beneficial effect of the drug may be the result of general reactions following its absorption into the body.

J. B. Millard

776. **Hydrocortisone in Lesions of Soft Tissue**
E. J. CRISP and P. H. KENDALL. *Lancet* [*Lancet*] **1**, 476–479, March 5, 1955. 3 figs., 12 refs.

Local injection of hydrocortisone was tried at Guy's Hospital, London, in the treatment of 208 cases of soft-tissue inflammation commonly termed " rheumatism ". Among the conditions treated were tennis elbow, golfer's elbow, plantar fasciitis, olecranon and pre-patellar bursitis, acute and chronic soft-tissue lesions of the shoulder-joints, tenosynovitis, and Dupuytren's contracture. A suspension of 25 mg. of hydrocortisone was mixed with 1,000 units of hyaluronidase dissolved in 2 to 5 ml. of 2% procaine hydrochloride, and the mixture injected into the area of greatest local tenderness. In 80% of cases there was complete relief of symptoms, in 10% there was a recurrence, usually in less than 3 months, and in 10% the treatment was ineffective. This treatment was also given in 29 cases of acute traumatic joint effusion with complete relief of symptoms (usually within 72 hours) in 21 cases, improvement in 7, and no change in one case.

[As the authors state, there is a natural history of spontaneous recovery in these conditions, although the period of painful incapacity is often long. A control series would have been of value.] *Oswald Savage*

RHEUMATOID ARTHRITIS

777. **The Value of Phenylbutazone in the Treatment of Rheumatoid Arthritis as Determined by Clinical Response and by the Serum Protein–Polysaccharide Ratio (PR)**
R. W. PAYNE, M. R. SHETLAR, C. H. FARR, A. A. HELLBAUM, and W. K. ISHMAEL. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **45**, 331–339, March, 1955. 13 refs.

The use of phenylbutazone (" butazolidin ") in the treatment of rheumatic disorders has tended to be discredited because the drug appears to have little influence on the erythrocyte sedimentation rate (E.S.R.) and the incidence of toxic reactions is high. Since the serum protein–polysaccharide ratio (PR) has been shown to reflect the degree of rheumatoid activity, it may be of objective value in assessing the results of therapeutic measures in rheumatic conditions. The authors, from the University of Oklahoma School of Medicine, report the results of a placebo-controlled investigation of the comparative effects of phenylbutazone and cortisone on the PR in 61 patients suffering from various rheumatic diseases.

In patients with rheumatoid arthritis, during the active stage of which the PR is high, significant and comparable falls in the PR were obtained with phenylbutazone in daily doses of 200 to 600 mg. and with cortisone in doses of 100 to 200 mg. Similarly in 3 patients with active ankylosing spondylitis, one with acute lupus erythematosus, and one with tophaceous gouty arthritis administration of phenylbutazone resulted in a reduction in the PR; when the drug was withdrawn there was a prompt exacerbation of clinical rheumatoid activity and a rise in the PR. The E.S.R. was of little aid, reflecting only very gross changes in the disease state. Toxic effects, mainly anaemia, a skin rash, and gastro-intestinal disturbances, were observed in 14% of the patients given phenylbutazone, but none of these reactions persisted after the drug was discontinued.

[The authors' conclusion that phenylbutazone can be prescribed with " a reasonable factor of safety " does not reflect the present general view in Britain.]

P. I. Reed

778. **Gold–Hormonal Therapy in Rheumatoid Arthritis**
P. J. BILKA and M. H. WEIL. *Annals of Internal Medicine* [*Ann. intern. Med.*] **42**, 638–643, March, 1955. 13 refs.

The aim of the investigation reported here from the University of Minnesota Medical School, Minneapolis, was to determine whether treatment with gold and cortisone combined was more effective than with either agent alone in rheumatoid arthritis. A series of 41 patients were given a minimum total dose of 500 mg. of aurothioglucose in combination with cortisone or corticotrophin therapy and were followed up for at least 3 months after cessation of hormone treatment. In 17% there was a complete remission, in 39% major improvement, and in 12% moderate improvement, the rest showing no change. These results are stated to approximate those obtained with gold alone. There were side-reactions to gold in 46% of cases. It is concluded that combined therapy has little to recommend it.

[From the data supplied and in the absence of any controls it is impossible to judge the validity of the authors' conclusions.]

G. Loewi

779. **Sensitization of Sheep Erythrocytes by Abnormal Human Serums. Clinical Value and Significance of Agglutination Reaction**
G. S. TAWIL and E. M. ABD EL WAHAB. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **25**, 166–174, Feb., 1955. 21 refs.

The agglutination of sensitized sheep erythrocytes is one of a number of agglutination tests which give positive results in a high percentage of sera from cases of rheumatoid arthritis. The authors, working at the Faculty of Medicine, Abbassia, Cairo, have investigated the specificity of the reaction and its diagnostic value in detecting the early stages of this disease. The technique is described in detail. Readings were made at one hour after incubation at 37° C., and at 18 hours at 15° C. Titres of 1 in 8 at one hour and of 1 in 32 at 18 hours were taken as the minimum values required for the result to be regarded as positive.

Of 100 sera sent for routine testing by the Wassermann reaction (W.R.), 72 failed to agglutinate in any titre, 16 agglutinated within the normal or negative range, 4 W.R.-positive and one W.R.-negative sera gave negative results, while 7 sera from cases of unrelated [?] conditions (bilharzia, discoid lupus erythematosus, and rheumatoid arthritis) gave positive results. In a second group of 48 cases diagnosed as rheumatoid arthritis, 38 (79%) gave positive results and 10 negative results. Of sera from 6 patients in whom rheumatoid disease had been present for less than 6 months, 5 gave positive reactions. Of 30 samples of serum from patients diagnosed as suffering from diseases other than rheumatoid arthritis [but including " rheumatic polyarthritis, menopausal arthritis, and gouty arthritis "], 25 gave negative and 5 positive results; of the latter, 3 were later reclassified as cases of rheumatoid arthritis, and the remaining 2 were diagnosed as cases of osteoarthritis of the knee and " recurrent rheumatic polyarthritis " respectively. A fourth group of 15 cases of various renal diseases gave 10 positive results, while in sera from 40 cases of rheumatic heart disease there were 34 with positive results. Lastly, sera from 15 cases of diverse hepatic disorders all reacted positively.

The authors discuss the nature of the reaction. The agglutination-enhancing action was in no way modified whether the sera were absorbed with washed sheep erythrocytes or sheep erythrocytes sensitized with amboceptor. Serum lipids play no part in the reaction, but it is suggested that a change involving protein metabolism in the liver is a significant feature. The rheumatoid factor responsible for these reactions is present in small amounts as a constituent of normal serum. The authors conclude that while the results of this test may be useful in confirming a diagnosis of rheumatoid arthritis, it cannot be considered in any way as specific for the disease.

Harry Coke

Physical Medicine

780. **Respiration and Speech in the Cerebral Palsied Child**
M. L. BLUMBERG. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **89**, 48–53, Jan., 1955. 1 fig., 5 refs.

After summarizing what is known at present concerning the neurophysiological links between respiration and speech, the author reports the results of speech training in 27 children with cerebral palsy under the care of the New York Department of Health. He has devised a simple apparatus for respiration training which is based on the principle of the water spirometer and which also enables the effect of such training, which is used in conjunction with conventional speech training, to be measured. He points out that spastic children without athetosis have better control of respiration, and therefore better quality of speech, than those with athetosis, whose hypothalamic centres are damaged. By combining training in breathing with training in speech good results can often be achieved, while at the same time the child's resistance to respiratory infections will, in theory, be increased. *L. Michaelis*

781. **Muscle Recovery in Poliomyelitis**
W. J. W. SHARRARD. *Journal of Bone and Joint Surgery* [*J. Bone Jt Surg.*] **37-B**, 63–79, Feb., 1955. 24 figs., 17 refs.

The author, at the Royal National Orthopaedic Hospital, London, set out to determine the extent of muscle recovery in poliomyelitis and the duration of the improvement, observing for this purpose the function of 3,033 lower-limb and 1,905 upper-limb muscles in 142 patients over a 3-year period.

The investigation showed that the rate of recovery of partly paralysed muscles was the same in both the upper and the lower limb. The ability of individual muscles to recover depended upon the proportion of muscles in the group which remained permanently paralysed. The rate of recovery was more rapid in children than in adults, and the amount of recovery which might be expected in a muscle could be predicted from a knowledge of its grade of muscle power at any time after one month from the onset of paralysis. The author found that fourteen-fiteenths of the total amount of recovery took place by the beginning of the twelfth month, and with rare exceptions individual muscle recovery was complete after 2 years. He also found that 90% of muscles which were still completely paralysed after 6 months usually remained permanently so. The prognosis for a totally paralysed muscle was related to the level of paralysis in muscles supplied by the same spinal segments. Deterioration in power in a muscle was uncommon and when it occurred it was associated with the " presence of the strong opposing force of antagonist muscles or of gravity ".

The application of these findings to the management of cases of paralytic acute anterior poliomyelitis is discussed. *Leon Gillis*

782. **The Relationship between Blood Flow, Capillary Surface Area and Sodium Clearance in Muscle**
D. N. WALDER. *Clinical Science* [*Clin. Sci.*] **14**, 303–315, May, 1955. 8 figs., 13 refs.

783. **The Rate of Blood Flow and the Oxygen Saturation of the Effluent Blood following Contraction of the Muscles of the Human Forearm**
A. H. G. LOVE. *Clinical Science* [*Clin. Sci.*] **14**, 275–283, May, 1955. 8 figs., 21 refs.

784. **Transmucosal Curare in the Rehabilitation of the Spastic Patient**
A. A. MARTUCCI, P. A. ANDERSON, E. W. JOHNSON, C. L. JOHNSTON, E. J. PEAR, and S. R. WEISS. *Journal of the Philadelphia General Hospital* [*J. Philad. gen. Hosp.*] **5**, 15–19, March, 1954 [received March, 1955].

D-Tubocurarine in tablet form in a dosage of 12 to 36 mg. daily was given sublingually to 9 spastic patients at the Philadelphia General Hospital and the effect on spasticity, pain, and movement was observed. Occasionally and at random a placebo was administered instead of the active drug. All the patients continued to receive physiotherapy while taking the drug. Brief clinical notes of the response to treatment in each case are given, and the results are summarized in a table [which, unfortunately, is very difficult to understand]. The authors state that D-tubocurarine administered sublingually was followed by a diminution in spasm, an increase in relaxation, relief of pain, and a greater range of mobility. Similar changes were observed in some cases when the inert tablet was given, and the authors suggest that this may have been due to the previous administration of the active preparation. No side-effects were observed in any case.

The authors admit that the series is too small for statistical evaluation. *W. Tegner*

785. **Acetic Acid Ionization. A Study to Determine the Abortive Effects upon Calcified Tendinitis of the Shoulder**
C. G. PSAKI and J. CARROLL. *Physical Therapy Review* [*Phys. Ther. Rev.*] **35**, 84–87, Feb., 1955. 4 refs.

The results of treatment of 12 cases of calcified tendinitis of the shoulder, based essentially upon ionization with an acetic acid solution, are reported. The condition affected one or both shoulders, and was characterized by local, non-radiating pain and joint tenderness, restriction of movement, stiffness, restlessness, and insomnia, and the diagnosis was confirmed radiologically in each case.

The technique employed was the " application of the negative pole of the galvanic current by ion-transfer with an acetic acid solution of 3%" to the affected shoulder. The current, at first low to break the skin threshold, was gradually increased to the limit of the subject's tolerance (usually between 5 to 10 mA), and retained at that level for 30 minutes. This was followed by application of a slowly alternating, sinusoidal, surging current to all muscles of the shoulder-girdle and upper arm for 5 minutes. Finally, when the subject became able to raise the arm, therapeutic exercises were prescribed. Treatment was given 3 times a week for 2 weeks, and then twice a week for 4 weeks.

In all cases, both acute and chronic, complete absorption of calcified deposits eventually took place. Pain, movement and tenderness all improved and in some cases disappeared within 2 to 6 weeks of starting treatment; the more chronic cases retained some limitation of movement. Moderate hyperaemia of the skin persisted for some three hours after each treatment.

[Even though the report deals with only 12 cases, the good clinical results and the absorption of calcified deposits in every case of a condition which is usually resistant to treatment seem worthy of note and should be confirmed. The hypothesis on which the method is based is perhaps somewhat tendentious, and some of the technical details, such as applying the positive pole to the surface of the back " with an infra-red lamp superimposed ", somewhat unorthodox.] *Harry Coke*

786. **Influence of Centripetal Rhythmic Compression on Localized Edema of an Extremity**

K. G. Wakim, G. M. Martin, and F. H. Krusen. *Archives of Physical Medicine and Rehabilitation* [*Arch. phys. Med.*] **36**, 98–103, Feb., 1955. 15 refs.

Oedema of the arm commonly follows radical mastectomy in obese patients and is mainly due to lymphatic obstruction; oedema of the leg may follow fracture or other trauma. Both these conditions are difficult to treat and the authors, writing from the Mayo Clinic, describe a method of treatment which is a helpful addition to the usual physiotherapeutic measures. This consists essentially in applying, for 2 half-hour periods daily, centripetal rhythmic compression to the oedematous limb by means of a pressure pump which inflates consecutively a series of 14 rubber cuffs placed round the limb to a pressure of 50 to 80 mm. Hg and at a rate of 20 waves per minute.

In a small series of 11 patients so treated the blood flow to the swollen and normal limbs was measured before and after treatment by a venous-occlusion plethysmograph fitted with a compensating spirometer recorder. The cutaneous circulation of the limbs was assessed by measuring the change in skin temperature by means of a thermocouple, and the circulation in a phalanx was measured by recording the pulse amplitude on a digital plethysmograph. The limb volume was measured before and after treatment by the method of fluid displacement. The results showed no consistent difference in the blood flow, skin temperature, or amplitude of the digital pulse as between the normal and swollen limb either before or after treatment, although clinically the oedema gradually subsided. At the end of treatment the volume of the swollen limb had decreased by 50 to 300 ml., pain was less, and the skin consistency and colour had usually become normal. The authors discuss the possible mechanism of oedema. *J. B. Millard*

787. **Low Back Pain Treated by Manipulation. A Controlled Series**

A. B. Coyer and I. H. M. Curwen. *British Medical Journal* [*Brit. med. J.*] **1**, 705–707, March 19, 1955. 6 refs.

A controlled investigation into the value of manipulation in the treatment of low back pain is reported. A total of 152 patients at St. Thomas's Hospital, London, were divided into two groups without selection, one group being treated by manipulation of the lumbar spine by the method of Cyriax, and the other (control) group by rest in bed and administration of analgesics. No fewer than 16 of the 76 control patients defaulted.

The authors found that 38 of the 76 patients given manipulation were free from signs and symptoms at the end of a week, whereas only 16 of the control group were free from pain and disability at this time. At the end of 6 weeks 9 in the former group still had signs and symptoms, compared with 17 in the latter. The authors consider their findings to indicate that manipulation is a logical method of treatment of the patient suffering from low back pain.

[This paper has aroused much interest and controversy. The fact that 16 out of 76 patients in the control group defaulted has led some observers to question the validity of the authors' results.] *W. Tegner*

788. **Physiological Effects of Generalized Heat Treatments**

W. S. McClellan and W. E. Lawrence. *British Journal of Physical Medicine* [*Brit. J. phys. Med.*] **18**, 59–63, March, 1955. 7 refs.

At the Spa, Saratoga Springs, New York, 30 male patients suffering from some form of rheumatic disorder were observed while receiving heat treatment in an electric-light cabinet. The treatment consisted in exposure for 20 minutes in a cabinet at 100° to 140° F. (37·8° to 60° C.), followed by a cooling douche. The body temperature rose to between 99° and 100° F. (37·2° and 37·8° C.) and the pulse rate rose by 10 to 40 beats a minute. The changes in blood pressure were slight. Estimation of the haemoglobin level and the blood count showed an increase in these values in some cases, and a decrease in an equal number of cases. As a result of this treatment many patients experienced relief of pain and increased joint movement, this improvement persisting for several months.

The authors review the literature, especially the work of Ott, who considered that the response to general heating was related to changes in the autonomic nervous system. It is suggested this treatment produces a fundamental change in the cells or the glands of the body which allows the patient to meet the stress of the underlying disease condition. *J. B. Millard*

Neurology and Neurosurgery

789. **The Use of Frequency Analysis in the Interpretation of the EEGs of Patients with Psychological Disorders**
M. A. KENNARD, M. S. RABINOVITCH, and W. P. FISTER. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] **7**, 29–38, Feb., 1955. 5 figs., 16 refs.

Analyses provided by an Offner frequency analyser [knowledge of the properties of which has unfortunately been assumed] of electroencephalograms from 3 groups of subjects have been plotted in an unusual way, 8 frequency patterns, derived from 4 positions on each side of the head from front to back, being superimposed. Significant differences were found between normal subjects, schizophrenics, and psychopaths (prison inmates) in that in the normal subjects and psychopaths the 8 curves followed the same general trends, whereas in the schizophrenics there was a tendency to disorderly scatter.

Fast activity was common to all groups, particularly when the subject was anxious, but activity above 20 c.p.s. was present to a significant degree only in those psychologically disordered subjects who showed anxiety to a marked degree. The prominence of theta activity noted by Hill in the electroencephalograms of psychopaths was confirmed. *W. A. Cobb*

790. **Disseminated Sclerosis. Pathogenetic Considerations and Therapeutic Possibilities.** (Multiple Sklerose. Pathogenetische Überlegungen und therapeutische Möglichkeiten)
F. GEORGI and A. BEUTHIEN. *Confinia neurologica* [*Confin. neurol. (Basel)*] **15**, 32–62, 1955. Bibliography.

The authors report the results of metabolic studies carried out in more than 100 cases of disseminated sclerosis at the Neurological Polyclinic of the University of Basle. Disturbance of liver function, as indicated by the hippuric acid excretion tests of Quick and by decreased availability of glycine, was found in 50 (60%) of 84 cases in which the diagnosis of disseminated sclerosis was clinically certain, while in a further 8% an abnormal result was obtained on repeating the tests. Interpreting these findings as indicating impairment of the detoxicating capacity of the liver, the authors conclude that the treatment of disseminated sclerosis with the salts of heavy metals is definitely contraindicated. They have themselves tried the effects of a regimen designed to support the liver—a high-protein, low-fat diet, together with supplements of methionine, choline, and vitamin B —on 52 patients suffering from the disease, with gratifying results. Such treatment may be of assistance even in long-standing cases by reducing spasticity. A close correlation exists between general clinical prognosis and the availability of glycine.

[This is a long, well-reasoned, and interesting paper which should be consulted in the original.]
J. B. Stanton

791. **Changes in the Skull in Myotonia Atrophica.** (Über Schädelveränderungen bei der myotonischen Dystrophie)
O. HALLEN. *Deutsche Zeitschrift für Nervenheilkunde* [*Dtsch. Z. Nervenheilk.*] **172**, 467–481, 1955. 7 figs., bibliography.

On radiographs of the skull of 33 patients seen at the University Neurological Clinic, Heidelberg, suffering from myotonia dystrophica the author measured the sella turcica and found it smaller than normal, as had previously been demonstrated. He also found local or general hyperostosis of the skull in 21 of the 33 cases and considers that these changes are further evidence of hormonal anomalies which may be important factors in the causation of this disease. *L. Michaelis*

792. **The Differential Diagnosis of Flaccid Paralysis**
P. H. SANDIFER. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **48**, 186–189, March, 1955. 2 figs., 29 refs.

In an admirable review of some of the less common causes of flaccid paralysis the author emphasizes that the clinical syndrome of amyotonia congenita may be caused by a variety of pathological processes; the commonest is a degenerative process in the anterior horn cells, but in some cases a congenital myopathy may be the cause. He also discusses the form of polymyositis simulating muscular dystrophy, the distal type of myopathy, the myopathic nature of cases of chronic progressive ophthalmoplegia, and the muscle wasting found in occasional cases of myasthenia gravis.
J. W. Aldren Turner

BRAIN AND MENINGES

793. **Observations on the Motor System following Cerebral Hemispherectomy**
L. A. FRENCH and D. R. JOHNSON. *Neurology* [*Neurology*] **5**, 11–14, Jan., 1955. 1 fig., 4 refs.

The effects of cerebral hemispherectomy on the motor function in a series of 8 patients with intractable convulsive seizures and hemiparesis occurring at an early age in life are reported. There seems to be no permanent deficit in motor function produced by this operative procedure. The caudate nucleus does not seem to be necessary for the integrity of the motor function of the contralateral extremities. Immediately postoperative the involved extremities are flaccid, but over a period of many months they again become spastic comparable to their preoperative status. Abdominal reflexes are not abolished by hemispherectomy. It is believed that the rapid return of motor function to the preoperative level is due to the contralateral hemisphere having assumed the function of the pathologic side many years pre-

operatively. It is felt that the pathologic hemisphere offers only a restraining effect on the motor function of the normal side.—[Authors' summary.]

794. **Diagnostic Localizing Value of Muscle Atrophy in Parietal Lobe Lesions**
A. SILVERSTEIN. *Neurology* [*Neurology*] **5**, 30–55, Jan., 1955. 28 figs., 45 refs.

In support of his thesis, discussed in several earlier papers, that muscular atrophy is a significant manifestation of disease of the parietal lobes the author, in this paper from Temple University Medical School, Philadelphia, analyses the incidence of atrophy in three groups of cases. Group 1 contained 10 cases of tumour of the parietal lobe in all of which there was the triad of atrophy, flaccidity, and cortical sensory loss, muscular atrophy being an important clinical feature. Group 2 included 30 cases of infantile cerebral lesions, chiefly porencephaly, with hemiplegia, atrophy, sensory loss, and convulsive seizures as the outstanding clinical features. Group 3 contained 50 cases of hemiplegia divided into two subgroups: (*a*) 28 cases with atrophy in the paralysed limbs which was associated with hypotonia and sensory loss, especially astereognosis; (*b*) 22 cases without atrophy or sensory loss but in which a spastic paralysis was usually present.

The author's conclusions are summarized as follows: "(1) Atrophy was strikingly evident in patients with tumors of the parietal lobe, while it was absent in cases where the frontal, temporal, and occipital lobes were affected. (2) Atrophy appeared promptly, together with other signs of the parietal syndrome, following surgical injury of the parietal region or invasion of it by lesions expanding from adjacent areas. (3) Unilateral atrophy has occurred as an isolated sign of parietal involvement, which refuted the argument that atrophy occurs only with pyramidal tract signs. (4) Atrophy has been observed as the earliest sign of parietal involvement, preceding sensory and motor disturbances. (5) Topical localization within the parietal lobe, similar to the pattern existing in the motor and sensory cortex, is borne out by several cases in which the atrophy was limited to the lower limb, face, and tongue. The upper limb is most frequently involved. (6) The degree of tissue wasting depends upon the size, character, and location of the lesion. Early atrophy is more easily detected by palpation of soft boggy muscles, pallor and smoothness of the skin and lessening of the finger lines—the "lady-like" hand. The most intense degree of wasting occurs in expanding cortical lesions affecting the motor pathways as well as the sensory cortex. In such instances there is a characteristic triad of atrophy, flaccid paralysis, and cortical sensory loss, especially astereognosis. The electrical reactions show a hypoexcitability to both faradic and galvanic stimulation, but no qualitative changes. (7) Subluxation of the shoulder due to muscular atrophy may produce synovitis and arthritis in hemiplegia. This fact would seem to be of therapeutic significance. (8) Abundant evidence in the old and new neurological literature confirms the concept of parietal amyotrophy . . . It is concluded that amyotrophy is a significant localizing sign of great value in the diagnosis of lesions of the parietal lobe. It is especially important when studying patients with a clouded sensorium . . . and to the neurosurgeon in directing an accurate operative exposure." *J. MacD. Holmes*

795. **Procaine Injection of the Prefrontal Lobe of the Brain: Technic and Present Indications**
R. SOUPAULT and M. BUCAILLE. *Annals of Surgery* [*Ann. Surg.*] **141**, 388–397, March, 1955. 5 figs., 27 refs.

A technique of procaine injection of the prefrontal lobes of the brain by means of a stereotaxic apparatus is described and the indications for this procedure are discussed. The authors then report the results obtained in cases of intractable pain, in certain severe diseases of the digestive tract, and in psychotic disorders such as the obsessive-compulsive states. Of the 35 patients with intractable pain, all except 3 improved, 14 markedly so. Satisfactory results were obtained in 8 patients with alimentary-tract disorders, including duodenal ulcer and ulcerative colitis, and in 2 patients suffering from obsessive-compulsive states. The authors consider that satisfactory results depend on accurate infiltration of the medial quadrants of the prefrontal lobes and that unilateral injection may be sufficient. *J. B. Stanton*

796. **The Symptoms Caused by Recent and Remote Injuries of the Frontal Lobes.** (Zur Symptomatik frischer und alter Stirnhirnverletzungen)
C. FAUST. *Archiv für Psychiatrie und Nervenkrankheiten* [*Arch. Psychiat. Nervenkr.*] **193**, 78–97, 1955. 7 figs., bibliography.

A follow-up study of 80 cases, both military and civilian, of penetrating injury of the frontal lobes of the brain is reported from the Psychiatric and Neurological Clinic of the University of Freiburg. The patients were all visited in their home surroundings and full account was taken of their occupational adaptation and family relations.

There were marked differences in the clinical picture between the older and the more recent cases, and between cases of injury of the convexity of the frontal lobe and of its basal, orbital part. Patients with orbital injuries were restless and without staying power, made excessive claims, were facile in discussing their difficulties in life, tactless, disinterested, reckless, and aggressive. Those with injuries of the convexity showed weakness or lack of initiative and drive, were easily distracted by outside influences, lacked self-criticism, and were persistently either euphoric or depressed. Whereas the former were intellectually unimpaired, the latter showed considerable poverty of ideas and difficulties in calculation and in the more complex processes of thought.

No patient with bilateral frontal injuries was capable of regular work, and indeed all the patients found it very difficult to remain in continuous employment. Over 40% of the patients had suffered from seizures at some time after their injury, but even when these occurred regularly they did not greatly impair employability. Ten patients had been charged with some criminal offence since the injury.

[Although this work is to a large extent a confirmation of earlier observations, of which it contains a full survey, its thoroughness and excellent documentation make it valuable, especially in view of the frequency with which the frontal lobe is nowadays deliberately traumatized in the performance of prefrontal leucotomy and similar operations.] *W. Mayer-Gross*

797. **Studies in Cerebrovascular Disease. I. The Syndrome of Intermittent Insufficiency of the Basilar Arterial System**

C. H. MILLIKAN and R. G. SIEKERT. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **30**, 61–68. Feb. 23, 1955. 7 refs.

The authors describe the syndrome of intermittent insufficiency of the basilar arterial system and report 10 cases, the symptoms indicating transitory impairment of function in some portion of the pons, mesencephalon, or occipital lobes. The clinical picture of complete occlusion of the basilar artery developed subsequently in 3 cases and the diagnosis was confirmed at necropsy. The transient symptoms which occurred in the attacks included amblyopia, diplopia, ptosis, confusion, clouding of consciousness, hemiparesis, dysarthria, dysphagia, unilateral sensory phenomena in the face, limbs, or trunk, vertigo, tinnitus, vomiting, and headache. Sometimes these symptoms were manifest on one side of the body during one attack and on the other side subsequently. The authors suggest that when this change of location is combined with visual-field disturbances, dysarthria, dysphagia, or vertigo, and when the symptoms are sharply episodic, a diagnosis of intermittent insufficiency of the basilar arterial system "is probably correct". They believe the attacks to be due to temporary insufficiency of blood flow through the basilar arterial system, but do not reach any firm conclusion concerning aetiology; atherosclerosis is clearly an important factor, but vascular spasm seems unlikely to be the cause. Whatever the aetiology, patients suffering from this syndrome should receive prolonged anticoagulant therapy; in some of the authors' cases the attacks ceased after administration of anticoagulants. *John N. Walton*

798. **Surgical Treatment of Internal Carotid Thrombosis**

A. DE SOUSA PEREIRA. *Annals of Surgery* [*Ann. Surg.*] **141**, 218–233, Feb., 1955. 12 figs., 9 refs.

This paper from the University of Oporto is based upon the author's experience in 31 cases of thrombotic obliteration of the internal carotid artery or its branches. In efforts to improve the circulation in the ischaemic areas, revascularization of this area through a temporal muscle graft was attempted in 2 cases without sucess, and carotid–jugular anastomosis was equally unrewarding in another 2 cases. Further, in no one of the 31 cases was the carotid thrombosis so situated and localized as to permit of replacement of the obliterated segment by a vascular graft, and attempts to open up the obliterated vessel failed and led to resection and ligation.

Only two procedures were found to be of value. Resection of a portion of the obliterated internal carotid artery (equivalent to a perivascular sympathectomy) and bilateral superior cervical sympathectomy were followed by clinical and angiographic evidence of improvement in 4 patients. The other procedure, which the author found of benefit to some patients, was an attack on the cerebral vasomotor pathways by means of a bilateral inferior cervical sympathectomy and perivascular sympathectomy or a bilateral superior cervical sympathectomy and perivascular sympathectomy, or in some cases by a combination of an inferior cervical and perivascular sympathectomy on one side and a superior cervical and perivascular sympathectomy on the other side with ligation of the external carotid artery. This last should be carried out on the side of the vascular occlusion in cases of thrombosis of the anterior or middle cerebral arteries, but where there is complete thrombosis of the internal carotid artery the ligation should be carried out on the opposite side, since here diversion of blood from the external to the internal carotid of the diseased side cannot occur. The variability of the results is, in the author's view, due in part to the variability of the anatomy of the circle of Willis, in which ten different types of vascular arrangement have been described, the generally accepted "normal" type occurring in only 20% of cases.

[There is much of interest in this paper. It remains to be shown to what extent revascularization of an area of the brain rendered ischaemic for more than a few hours is possible, and if so how far such revascularization can reduce a severe functional deficit of any duration. Further, clinical improvement after various therapeutic procedures in cases of hemiplegia due to carotid thrombosis may be no more than would have occurred without specific treatment. Ability to walk and movement at the proximal joints of the affected upper limb are results to be expected with proper rehabilitation of the severely hemiplegic.] *J. E. A. O'Connell*

799. **Primary Cerebral Hydatid Disease**

H. R. DEW. *Australian and New Zealand Journal of Surgery* [*Aust. N.Z. J. Surg.*] **24**, 161–171, Feb., 1955. 11 figs., 4 refs.

The author first summarizes present views of the characteristics of primary cerebral hydatid disease as follows: primary cysts are solitary and adventitial capsule is scanty or absent; the condition commonly occurs in young children, is slowly progressive, and usually manifests itself by the age of 10 years; skull thinning or perforation may be noted and the Casoni and complement-deviation tests are unreliable. He then briefly describes and comments on 10 cases, some of which have already been reported. The more complete picture which these 10 cases present emphasizes certain variations from the "normal". While cysts are usually single, more than one may be found and the adventitial capsule may be thick or even calcified. Daughter cysts are not uncommon and may be related to trauma. Ventricular puncture should be undertaken with care when hydatid disease is suspected; if the side of the lesion can be determined by clinical means then ventriculography should be undertaken by puncture of the opposite ventricle only. Most cysts are large—average 10 cm. in diameter—so that a very wide exposure at operation is advisable. The

cyst should be uncapped, partially evacuated, and filled with 5% formalin, which is allowed to act for three minutes and then carefully sucked out and the cavity cleansed; the cyst is then removed. The author emphasizes that evacuation and fixation may prove difficult when daughter cysts are present. *Brodie Hughes*

800. **Recent Developments in the Management of Brain Abscess**
W. LEWIN. *British Medical Journal* [*Brit. med. J.*] 1, 631–634, March 12, 1955. 10 refs.

At the Radcliffe Infirmary, Oxford, the mortality from brain abscess has steadily fallen in recent years: in 1938–43, before the advent of penicillin, 22 out of 48 patients died (46%); in 1944–8 out of 62 patients, 18 died (29%); but in 1950–4 only 7 out of 36 died (19·4%). Analysing the factors responsible for these improved results the author points out that while the introduction of antibiotics was of outstanding importance, superior methods of location, coupled with experience in the methods of treatment available, also contributed. Metastatic abscesses from a focus in the lung are the most frequent cause of death, but many cases have recently been successfully treated and the affected lung removed to lessen the risk of a recurrence of the abscess; in this connexion the author cites the series reported by Pennybacker and Sellors (*Lancet*, 1948, **2**, 90; *Abstracts of World Surgery*, 1949, **5**, 92).

It is pointed out that the early use of penicillin may so mask the active and very dangerous invasive stage that a diagnosis of cerebral abscess may be rejected on the grounds that the patient is not sufficiently ill. Ancillary methods of investigation such as electroencephalography and angiography are valuable, but in some cases they yield equivocal results; a sound clinical appreciation of the case remains the first essential in diagnosis. Lumbar puncture may be invaluable, but caution is advised in the use of this procedure because of the risk of tentorial impaction. The treatment of choice in the acute stage is intermittent aspiration of the abscess, combined with local and systemic administration of antibiotics, usually penicillin, but formal decompression may be required in some instances. At present " there is no one operation which is applicable to all cases of acute abscess; each case must be considered on its merits ". The risk of rupture into the ventricle and the presence of multiple abscesses remain major problems for the surgeon. As a final test of cure air encephalography should be carried out in the quiescent stage to ensure that no loculus remains, but this procedure is by no means infallible and large abscesses may remain undetected. The author favours injection of " thorotrast " into the abscess cavity at the time of aspiration; over a period of 14 years he has not observed any adverse effects from the use of this contrast medium.

Discussing excision, the author states that apart from those cases in which excision is necessary in the acute stage, there are others in which pus continues to re-accumulate despite repeated aspiration; if there is the slightest doubt whether infection has resolved excision of frontal, temporal, and cerebellar abscesses is advisable. In the period 1950–4 he excised abscesses in 18 out of the 29 patients who survived the acute stage, without mortality.

Epilepsy is a sequel in 45% of patients who recover from brain abscess, the incidence being highest in those with multiple or frontal abscesses; it is seldom so marked, however, that the patient cannot lead a fairly normal life with the aid of anticonvulsant drugs. The author suggests that the possibilities of surgical excision of scar tissue, with the help of electrocorticography, particularly in the frontal region, merit further attention.
D. P. McDonald

801. **Evaluation of Ocular Signs and Symptoms in Verified Brain Tumors**
J. F. O'ROURKE and N. S. SCHLEZINGER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **157**, 695–700, Feb. 26, 1955. 7 figs., 19 refs.

An evaluation is presented of the ocular signs and symptoms in 100 verified cases of brain tumour which were initially admitted to Wills Eye Hospital, Philadelphia, and subsequently referred to a neurosurgeon. As a result of this selection the incidence of various types of tumour was unusual, pituitary tumours being present in 24 cases, meningiomata in 21, and gliomata in 18. Optic atrophy was observed in 58 cases and papilloedema in 42, so that ophthalmoscopic evidence of value was available.

All the patients with pituitary tumours had field defects and a visual acuity of less than 6/60 in one eye. [No close consideration is given to the type of field loss.] The meningiomata were situated in the region of the sella turcica, being parasellar, suprasellar, or subfrontal. Ten of the gliomata were in the cerebellum, the presenting sign being raised intracranial pressure. [No mention is made here of chiasmal field defects from distension of the third ventricle.] The other main conditions seen were intracranial spread of nasopharyngeal carcinoma in 10 cases and acoustic neurinomata in 8.

[The symptoms and signs encountered in this series are only very briefly described. They conform to the classic descriptions of signs and symptoms in the various types of tumour and no new syndromes emerge from this analysis.] *Brodie Hughes*

EPILEPSY

802. **Disorders of Smell, Taste, and Appetite in Psychomotor Epilepsy.** (Troubles de l'olfaction, de la gustation et de l'appétit chez les épileptiques psychomoteurs)
H. GASTAUT, J. ROGER, and C. GIOVE. *Annales médico-psychologiques* [*Ann. méd.-psychol.*] **1**, 177–206, Feb., 1955. 2 figs., 21 refs.

Recent anatomico-physiological studies in animals have shown that the rhinencephalic areas bordering the Sylvian fissure regulate the complex automatic activities which are concerned in the search for food, as well as in sexual activity and the gregarious life. The present authors have previously shown that patients with psychomotor epilepsy due to lesions of the rhinencephalon in

the peri-Sylvian region often suffer from disturbances of sexual and social activity. Since the peri-Sylvian region also contains the olfactory and gustatory centres it is reasonable to expect that disturbances of smell and taste should occur in psychomotor epileptics during and between their attacks. The authors have encountered olfactory and gustatory hallucinations, however, only 59 times in 1,000 patients, but they found it impossible in all cases to distinguish accurately between disorders of taste and smell. Purely gustatory hallucinations are very rare, but purely olfactory ones are more common, while mixed olfacto-gustatory hallucinations are less rare than the purely gustatory ones. In this paper they describe the associated psycho-sensory phenomena, such as dilatation of the nostrils, sniffing, movements of the tongue, and smacking of the lips. A common psycho-sensory accompaniment is the recalling of old memories—an example is given from Marcel Proust of a vivid memory he recalled after tasting a spiced cake dipped in tea. Several other kinds of sensory and psychomotor associations are described, illustrating that there is a great deal of variation in the pattern of psychomotor fits.

The authors distinguish clearly between hallucinations and illusions of taste and smell, and point out that although hallucinations are well described in the literature, there is little mention of illusions, that is, the abnormal interpretation of substances actually tasted. They have found two types of disorder of taste and smell in psychomotor epileptics in the intervals between the fits: the first is a deficiency—an inability to recognize common test substances; the second is irritative, either in the form of permanent hallucination or an exaggeration, hypergeusia or hyperosmia. The disorders of appetite found in their cases were a consequence of the disordered sense of smell and taste. *J. MacD. Holmes*

803. The Neurosurgical Treatment of Jacksonian Epilepsy Associated with Infantile Spastic Hemiplegia. (Il trattamento neurochirurgico della epilessia jacksoniana associata ad emiplegia spastica infantile)
M. MILLETTI. *Archivio di Neurochirurgia* [*Arch. Neurochir. (Bologna)*] **2**, 21–87, Jan.–March, 1954 [received March, 1955]. 35 figs., bibliography.

After a historical review of the problems of aetiology and classification of infantile hemiplegia with focal epilepsy, the author describes the various neurosurgical procedures which have been used in treating this condition and gives the histories and results in 15 such cases treated at the Ospedale Maggiore, Bologna. Among the aetiological factors in these cases were trauma, vascular occlusion, porencephaly, microgyria, and meningoencephalitis occurring in childhood. All the patients presented with a spastic hemiplegia of varying degree existing from birth or early childhood, which was associated with Jacksonian attacks of the affected limbs and more or less marked psychic changes.

In diagnosis radiography (including pneumoencephalography), electroencephalography, and arteriography gave useful information relating to the underlying lesion, and at operation electrocorticography was an important guide in most cases to the amount of brain tissue to be removed. Of the author's 15 patients, 11 were subjected to surgical procedures directed against the lesion responsible. These included division of cortico-meningeal adhesions, lobectomy, total excision of porencephalic cysts, and hemispherectomy. As a result 7 patients were greatly improved in respect of fits, hemiplegia, speech, and mental state, 2 were much improved, and one remained virtually unchanged; the eleventh patient died after hemispherectomy. The author concludes that the best results are achieved by limiting total hemispherectomy to cases in which the whole hemisphere is atrophic or shows abnormal electrical activity, and by restricting the operation in other cases to radical excision of the pathological tissue, using electrocorticography as a guide.
J. B. Stanton

804. Diuretics in Therapy of Epilepsy. Their Use for the Potentiation of Anticonvulsant Drugs
N. A. BERCEL. *California Medicine* [*Calif. Med.*] **82**, 107–110, Feb., 1955. 9 refs.

On the hypothesis that any substance which increases the permeability of the blood–brain barrier is likely to aid absorption of a drug by the brain, the author, at the University of Southern California, Los Angeles, studied the effect of the addition of diuretics to anticonvulsants in the treatment of epilepsy. Animal experiments are cited which showed that diuretics increased the protection afforded by anticonvulsant drugs against leptazol (" metrazol "). Ten patients suffering from epilepsy of various types in whom anticonvulsants in adequate dosage had a toxic effect were given 0·3 g. of theobromine, with or without 0·09 to 0·15 g. of phenobarbitone or theophylline, 2 or 3 times daily in addition to the usual anticonvulsant drugs. The average number of seizures each month, determined over a 6-month period before the diuretic was given, was compared with that over a similar period when diuretics were administered. In all cases the addition of the diuretic permitted a reduction in a previously toxic dosage of an anticonvulsant drug without lessening the control of the seizures; in some cases control of seizures improved. In 3 cases excessive diuresis and gastric discomfort were encountered.
J. B. Stanton

SPINAL CORD

805. Basilar Impression
D. G. PHILLIPS. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **18**, 58–67, Feb., 1955. 10 figs., 14 refs.

A study of radiographs of the skull of 612 patients admitted to Frenchay Hospital, Bristol, over a 4-year period revealed 8 cases of basilar impression, the criterion on which the diagnosis was based being the arbitrary one of elevation of the odontoid tip 5 mm. or more above Chamberlain's line (a line from the posterior end of the hard palate to the posterior margin of the foramen magnum). A further 13 cases were diagnosed later. The condition was secondary to Paget's disease in one case and to osteitis of the atlas and axis in another; in the remainder it was congenital in origin and associated

with a high incidence of developmental anomalies such as fusion of the cervical vertebrae and occipitalization of atlas or odontoid. Symptoms, which had been present for periods varying from 2 months to 10 years, included suboccipital pain or stiffness, vomiting, loss of consciousness, cranial-nerve disorders, unsteady gait, urinary incontinence and pain, weakness, and paraesthesiae or numbness of the trunk and limbs. Among the abnormalities found were visible deformity of the head or spine, cranial-nerve palsy, nystagmus, ataxia, wasting of the upper limb, pyramidal-tract disorders, cutaneous sensory loss in the trunk or limbs, and papilloedema. Some patients were asymptomatic; in others symptoms improved spontaneously or responded to treatment with rest or immobilization in a cervical collar. Surgical decompression was carried out in about half the cases, usually those in which the neurological symptoms were progressive. Postoperative complications due to involvement of the medulla, respiratory tract, or cerebrospinal-fluid circulation were encountered in some cases.

I. Ansell

806. **Incarceration of the First Sacral Nerve in a Lateral Bony Recess of the Spinal Canal as a Cause of Sciatica**

P. T. SCHLESINGER. *Journal of Bone and Joint Surgery* [*J. Bone Jt Surg.*] **37-A**, 115–124, Jan., 1955. 7 figs., 17 refs.

The author points out that a bony recess normally exists in the spinal canal at the level of the fifth lumbar and first sacral vertebrae medial to the intervertebral foramen, its posterior wall being formed by the superior articular process of the sacrum and its anterior wall by the fifth lumbar disk and vertebral body. In some individuals this recess is very deep, so that occasionally the first sacral nerve may become incarcerated and compressed in it, causing severe sciatica.

Two such cases in middle-aged men are here reported from Glen Falls Hospital, New York, in both of which there was a history of fluctuating but progressive sciatic pain, restriction of movement, and neurological signs. Radiography showed degenerative disease of the disk and vertebrae, but the myelogram proved negative. At operation no herniation of the disk was found, but the first sacral nerve (which in its extrathecal course as it crosses the fifth lumbar disk is normally adjacent to the dura) was seen to lie far laterally and deep in the bony recess, being so tightly wedged that only with great difficulty could it be extricated. The recess was therefore eliminated by resection of part of the articular process of the sacrum and the inferior process of the fifth lumbar vertebra, the disk not being resected; both patients have remained free from further symptoms.

The depth and extent of the bony recess described depends on the arrangement of the articular processes of the 5th lumbar and 1st sacral vertebrae, the more the articular surfaces lie on a frontal plane the deeper the recess will be. In these circumstances narrowing of the disk will bring about compression of the sacral nerve in the recess or in the intervertebral foramen, which can be considered as a lateral prolongation of it. The author therefore suggests that the possibility of compression of the first sacral nerve in the manner described should be kept in mind in cases of sciatica in older patients who show radiological signs of degenerative disk disease with thinning, and that in these circumstances, when no protrusion of the disk is found on myelography or operation, the root should be explored and followed as far as the intervertebral foramen.

Richard de Alarcón

807. **Spinal Cord Compression Due to Spontaneous Epidural Hemorrhage. Report of Three Cases**

E. W. AMYES, P. J. VOGEL, and R. B. RANEY. *Bulletin of the Los Angeles Neurological Society* [*Bull. Los Angeles neurol. Soc.*] **20**, 1–8, March, 1955. 4 figs., 6 refs.

808. **Spastic Paraplegia of Middle Age. A Clinico-pathological Study**

J. MARSHALL. *Lancet* [*Lancet*] **1**, 643–646, March 26, 1955. 3 refs.

The main purpose of the investigation reported here was to obtain further information on the natural history of a type of spastic paraplegia of uncertain aetiology, commonly seen in middle-aged patients, in which there may be great difficulty in establishing a correct diagnosis even with the aid of the latest ancillary methods and with observation over a prolonged period of time. Cases were regarded as falling within this category when the paraplegia was of gradual onset after the age of 20 and of slow progression, and when a bilateral extensor plantar response was invariably present, with or without other signs of a pyramidal lesion, sensory loss, or sphincter disturbance.

The records of 80 such cases were found among those of patients examined at the National Hospital, Queen Square, London, between 1930 and 1952, and a further 35 cases were found among the necropsy records for the period 1928–52. In 52 of the former group the patient was traced, and 9 others were found to have died; the remaining 19 could not be traced. Most of the 52 patients were examined by the author and information regarding the others was obtained from the replies to a postal inquiry.

The diagnosis had become apparent in only 27 of the 52, remaining obscure in the rest in spite of repeated investigation. The average age of this group was 40 years at the time when symptoms had first appeared, and the duration of the illness at the time of follow-up averaged 10·4 years, being more than 5 years in most cases. Disseminated sclerosis accounted for 10 cases, spinal tumour for 7, and prolapsed intervertebral disk for 3; dementia developed after the paraplegia in 4 cases —the *paraplégie des vieillards* of Lhermitte. In the 35 cases obtained from necropsy records the findings were much the same. About one-third had disseminated sclerosis, one-third compression of the cord by a tumour or prolapsed disk, the remaining third including a heterogeneous group of conditions, some of them rare. In only 5 of the 87 cases in the combined groups was the paraplegia found to be consequent upon cervical spondylosis.

Adrian V. Adams

Psychiatry

809. **Psychical Phenomena in Temporal Lobe Epilepsy and the Psychoses**
S. KARAGULLA and E. E. ROBERTSON. *British Medical Journal* [*Brit. med. J.*] **1**, 748–752, March 26, 1955. 8 refs.

From a large series of cases seen at the Montreal Neurological Institute and the Royal Edinburgh Hospital for Mental and Nervous Disorders the authors have selected for description 5 cases of temporal lobe epilepsy in which the aura consisted of ill-defined or formulated thoughts, an inner " voice " which seemed to be within the head or abdomen, or an external voice. In 3 of these cases the phenomena could be reproduced by electrical stimulation of the cortex during craniotomy. There is a gradation, therefore, from " thoughts " to the fully formed auditory hallucination, and it is pointed out that a similar though more complex gradation is seen in schizophrenia. The authors feel that all the stages should be regarded as hallucinations. A study of 4 further cases of epilepsy showed that a similar gradation from internal to external perceptions occurred in patients with visual auras—and again parallel phenomena are found in schizophrenia.

As part of the thought process is the evocation of words and of visual images, it is not surprising that a physical stimulus may reproduce thoughts or a visual or verbal image. It is concluded that the similarity between temporal lobe epilepsy and schizophrenia in this respect suggests that there is a common neurophysiological basis for the phenomena described.

L. G. Kiloh

810. **Fatigue during the Second Six Months of Abstinence**
M. WELLMAN. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **72**, 338–342, March 1, 1955. 6 refs.

The control of fatigue following 6 months' abstinence in the patient who has developed intolerance to alcohol after attacks of alcoholic amnesia for 2 years is discussed. During the second 6 months of abstinence fatigue is the chief symptom, displacing to a large extent the earlier irritability, restlessness, and depression. It increases with work (mental or physical) but is disproportionately great, resembling fatigue in the aged or the chronic invalid. Emotional disturbance, tension, and the patient's own realization of his reduced capacity and, if he is married, of his diminished importance in the household increase this fatigue. Pursuing rehabilitation the patient tries to disregard his fatigue, but in so doing aggravates it, and thereby adversely influences the general syndrome.

In the author's view treatment during this period consists essentially in rest—sleep if possible—for not less than 10 hours in each 24. If necessary, sleep should be ensured by administration of sedatives, such as 0·2 g. of pentobarbitone sodium, on 3 successive nights in each week. In the case of a married person, an understanding by both partners of the underlying causes of domestic friction peculiar to this stage (including the subconscious struggle for control) should do much to reduce emotional tension. The knowledge that in spite of the symptoms this period is normally characterized by slow but steady improvement which is accelerated towards the end will greatly encourage the patient and the partner.

[This is an interesting paper worthy of further elaboration.] *R. J. Matthews*

811. **The Mortality of Morphine Addiction.** (Zur Sterblichkeit der Morphinisten)
E. RÜDIN. *Archiv für Psychiatrie und Nervenkrankheiten* [*Arch. Psychiat. Nervenkr.*] **193**, 98–116, 1955. 15 refs.

Very little statistical information has hitherto been available concerning the effect of morphine addiction on mortality and life expectation. The author has attempted to fill this gap by following up 348 cases of morphine addiction (222 in males and 126 in females) treated at the University Neurological Clinic and the Schwabing Municipal Hospital, Munich, between 1906 and 1940. At the time of their treatment for addiction about one-quarter of the patients were suffering from a severe physical illness likely to reduce their life expectation, but the others were physically healthy. The series contained a large proportion of relatively young patients: addiction started before the age of 40 in 83% of the patients, and 63% were treated for it before they reached that age.

Mortality in the series as a whole was 3 times higher than in the general population, and this was found to hold true for all the categories into which the patients were subdivided. It was slightly less among female than among male addicts, but the difference in mortality between patients who were physically ill and those without physical disease was insignificant. Among the causes of death, suicide occurred in 16% of cases, while in 20% of the whole series some connexion with the addiction was evident in such causes as accidents, marasmus, and furunculosis. *W. Mayer-Gross*

812. **The Serum Cholesterol and Lipoprotein Levels in Mongolism**
C. E. BENDA and G. V. MANN. *Journal of Pediatrics* [*J. Pediat.*] **46**, 49–53, Jan., 1955. 12 refs.

A comparison of the serum total cholesterol levels and certain classes of serum *beta*-lipoprotein levels among 54 mongoloid subjects, 54 institutional controls, and 1,039 well subjects has failed to reveal consistent differences. Such evidence of higher serum lipid levels as was found among the mongoloids appears to b

explained by a greater prevalence of obesity in those subjects. Mongolism is not characterized by unusual serum lipid patterns.—[Authors' summary.]

813. **A Possible Mechanism for Disturbance in Tyrosine Metabolism in Phenylpyruvic Oligophrenia**
J. DANCIS and M. E. BALIS. *Pediatrics* [*Pediatrics*] **15**, 63–66, Jan., 1955. 1 fig., 7 refs.

TREATMENT

814. **The EEG Changes in Unilateral and Bilateral Frontal Lobotomy**
R. D. WALTER, C. L. YEAGER, L. H. MARGOLIS, and A. SIMON. *American Journal of Psychiatry* [*Amer. J. Psychiat.*] **111**, 590–594, Feb., 1955. 1 fig., 7 refs.

At the University of California School of Medicine, San Francisco, the authors have made a study of the changes in the electroencephalogram (EEG) following leucotomy, the duration and reversibility of these changes, and their correlation with clinical improvement in a series of 150 patients (125 with schizophrenia, 14 with involutional melancholia, 5 with manic depression, 4 with obsessive-compulsive neurosis, and 2 with psychosis and epilepsy). Of these, 117 underwent bilateral and 54 unilateral operation, 27 on the left side and 27 on the right. Many of the patients had two separate unilateral operations, the second on the opposite side 4 to 7 months after the first. Only cases with adequate pre- and post-operative EEG recordings were selected. In all cases EEG recordings were made preoperatively and 9 days postoperatively and then at intervals for as long as the patients could be followed up, in some cases up to 3 years.

The recordings made 9 days after bilateral leucotomy showed high-potential random activity at 1 to 4 c.p.s. In 100 of the 117 cases it was more prominent in the frontal areas, but in only 21 was it exclusively restricted to these leads; in 19 cases there was fronto-temporal and in 5 fronto-parietal slowing. In 8 cases the greatest degree of slowing was obtained from the temporal rather than the parietal areas. At 6 weeks after operation the EEG records had become more focal in the frontal leads and the previously noted temporal and parietal slowing had disappeared. Of 42 patients followed for one year, only 5 had a normal EEG, the remainder showing mainly mild to moderate slow activity limited to the frontal areas. After 2 years 27 out of 29 showed slow frontal activity, and after 3 years 17 out of 19 (89·5%) still had frontal slowing.

After unilateral leucotomy, 26 out of 34 patients showed focal slowing on the operated side at 9 days; in 4 cases the slowing was equal on both sides and in 4 it appeared on the opposite side. After 2 or 3 months the EEG records were indistinguishable from those of patients undergoing bilateral operation. Of 8 patients who had two separate unilateral leucotomies, 7 showed frontal slowing on both sides 2 to 3 years after the second operation. In regard to complications, 10% of the bilaterally operated patients developed seizures. The preoperative tracings of these patients showed no paroxysmal dysrhythmia, but records taken 6 to 9 months after operation showed definite paroxysmal activity in 10 out of 17.

The authors conclude that there is a definite correlation between the degree of early postoperative slow activity in the EEG and clinical improvement. Patients with moderate slowing showed greater improvement than those with slight or severe slowing. They suggest that the degree of slowing is related to the extent of the operation, slight slowing indicating that the operation was not extensive enough, while severe slowing would suggest that it was too extensive.

Richard de Alarcón

815. **Insulin Coma Therapy in Schizophrenia. A Fourteen-year Follow-up Study**
F. H. WEST, E. D. BOND, J. T. SHURLEY, and C. D. MEYERS. *American Journal of Psychiatry* [*Amer. J. Psychiat.*] **111**, 583–589, Feb., 1955. 10 refs.

The authors report on the immediate and long-term results of insulin-coma therapy in a series of 781 mental patients treated at the Pennsylvania Hospital, Philadelphia, between 1936 and 1951, of whom all but 42 were schizophrenics. Coma was induced on 5 days a week for 1½ to 2 hours daily, the number of comas being determined by the degree of clinical improvement. The average course lasted 3 months and involved a total of 60 to 90 hours of coma. Electric convulsion therapy (E.C.T.) was used conjointly in those cases which did not improve significantly after the 13th coma. Whenever possible patients were discharged within a week of the last treatment. Follow-up information was obtained by letter from relatives, physicians, and in some cases from other hospitals.

The immediate results of treatment, graded on a 3-point scale, were: improved or recovered 67·7%, slightly improved 7·9%, and unimproved 23·9%. After 5 years the proportion showing a continuously favourable course fell to 32·2%, and after 12 years to 26·8%; after 14 years only 20·4% of those followed up were still considered well or improved. Moreover, after 5 years only 12·5% had remained well without relapse or further treatment, but on the other hand only 15·6% remained ill without showing improvement, regardless of subsequent treatment. Of the patients who originally responded well, 63·3% had at least one relapse afterwards, 44% of these first relapses occurring within 30 days and 78% within the first year. This high relapse rate suggests that treatment with insulin does not reduce the likelihood of recurrence.

The immediate results were correlated with various factors of possible prognostic significance; in general the findings agreed with those of other workers. The sex of the patient or the conjoint administration of E.C.T. did not influence the results; patients aged 16 and under responded poorly, as also did hebephrenics; the longer the duration of the illness, the poorer the response to treatment. An increase in body weight during treatment, however, proved of good prognosis, the more weight gained, the better the outcome. The results in

this series were compared with those in a series studied before the use of insulin coma. The authors conclude that insulin-coma therapy increases the percentage of recoveries, renders psychotherapy easier, and shortens the time spent in hospital; it does not, however, prevent the possibility of relapse. *Richard de Alarcón*

816. Intensive Insulin Shock Therapy—a Five-year Survey

E. P. BRANNON and W. L. GRAHAM. *American Journal of Psychiatry* [*Amer. J. Psychiat.*] **111**, 659–663, March, 1955. 5 refs.

Between 1948 and 1953 at the Veterans Administration Hospital, Perry Point, Maryland, a total of 528 patients, the majority being male schizophrenics, received intensive insulin shock therapy. The average number of hours of coma per patient was 131·5, the average duration of treatment being approximately 57·3 days per patient. This was supplemented by intensive psychotherapy and, if necessary, electric convulsion therapy.

About two-thirds of the patients were fit to be discharged after treatment, but about one-quarter had to be readmitted. The recovery rate was higher in the younger than in the older age groups; it was highest in those treated within 6 months of the onset, diminishing progressively thereafter with the duration of the illness. The authors consider that patients who respond well should be discharged within 2 to 3 weeks of completion of treatment in order to prevent a relapse. *F. K. Taylor*

817. Treatment of Mental Disease by Sleep

O. V. KERBIKOV. *Lancet* [*Lancet*] **1**, 744–745, April 9, 1955. 13 refs.

The induction of deep sleep (as distinct from narcosis) as a therapeutic method is based on Pavlov's theory of protective cortical inhibition, and has been widely used in Russia in recent years, particularly in the treatment of patients with depressive-inhibitory states. The author here describes the various techniques employed in the Psychiatric Clinic of the Second Moscow Medical Institute.

"Electro-sleep" is induced by the rhythmic application of a weak electric current through electrodes in the orbito-occipital position for 2 hours daily in a total course of 10 to 20 treatments. It has proved beneficial in cases of neurosis and asthenic depression. Sleep induced by means of intravenous infusions of a 10 to 20% solution of alcohol, given daily for periods of 4 to 5 days with intervals of 1 to 2 days in a total course of 12 to 15 treatments, has produced good results in schizophrenia and in patients who refuse food. Other methods used are the daily injection of caffeine (0·2 g. intramuscularly) and soluble amylobarbitone (3 to 10 ml. of a 5% solution intravenously) in courses of 10 to 60 treatments, and the subcutaneous injection of 400 to 500 ml. of nitrous oxide daily in a course of 12 treatments. The action of the drugs is reinforced by monotonous repetitive stimuli (such as the sound of a muffled metronome or a flashing blue light), the application of heat, and the use of various other methods of inducing conditioned sleep.

F. K. Taylor

818. Uses of Chlorpromazine in Mental Hospital Patients

J. LOMAS. *British Medical Journal* [*Brit. med. J.*] **1**, 879–882, April 9, 1955. 14 refs.

Since November, 1953, nearly 500 psychiatric patients at Springfield Hospital, London, have been treated with chlorpromazine for periods varying from a few days to 6 months, and in this paper the results obtained in 205 (55 males and 150 females) treated before the end of March, 1954, are reported. At first the drug was given intramuscularly; later it was given by mouth in a dosage of 25 mg. three times a day for one week, increasing to 50 mg. in the second week and to 75 mg. thereafter. Intramuscular injections were given only to those patients who were too resistive to take drugs by mouth. Some patients improved in a few days: others needed several weeks' treatment. In the majority the maximum benefit was observed after 3 months; treatment was not abandoned, therefore, in less than 2 months but was rarely continued beyond 3 months.

Of the 205 patients, 9 died during treatment, but chlorpromazine was not considered to be in any way responsible for death. The results in the remaining 196 patients are given in the following table.

Diagnosis	Recovered	Much Improved	Moderately or Slightly Improved	Unimproved	Total
Schizophrenia	4	17	78	37	136
Endogenous depression	2	4	6	7	19
Neuroses and psychopathic states	2	6	3	7	18
Organic states	—	—	11	5	16
Mania and hypomania	1	—	4	2	7
Total ..	9	27	102	58	196

Although relapse occurred when the drug was withdrawn, rehabilitation became possible in patients who were previously too disturbed for this to be attempted. When the results were related to the duration of stay in hospital before treatment started, it was found that of 93 who had been in hospital for 1 to 6 months, 22 did not improve; of 38 who had been in hospital 6 to 24 months, 12 were unimproved; while of 65 who had been resident for over 2 years, 24 did not improve. Analysis of the results according to the psychomotor state showed that of 126 overactive patients, 35 failed to benefit from chlorpromazine; of 52 inhibited patients, 21 did not respond; and of 18 inhibited patients with impulsive outbursts, 2 were unimproved.

Of 28 patients who had been subjected to leucotomy, 8 did not respond to administration of chlorpromazine.

G. de M. Rudolf

819. Treatment of Psychotic States with Chlorpromazine

D. GOLDMAN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **157**, 1274–1278, April 9, 1955. 6 refs.

Dermatology

820. **Erythrodermia with Lipomelanic Reticulum-cell Hyperplasia of Lymph Nodes (Dermatopathic Lymphadenitis)**
R. C. NAIRN and T. E. ANDERSON. *British Medical Journal* [*Brit. med. J.*] **1**, 820–824, April 2, 1955. 12 refs.

Writing from the University of Aberdeen, the authors describe in detail 13 cases of erythrodermia accompanied by hyperplasia of lymph nodes in 6 patients (3 men and 3 women) with generalized exfoliative erythrodermia, 4 (2 men and 2 women) with exfoliative psoriasis, 2 women with Besnier's prurigo and ichthyosis, and one man with reticulosis.

The histological changes in the enlarged lymph nodes were as follows. Reticulum-cell hyperplasia was found in all specimens, and in all but 2 there was reactive lymphoid hyperplasia which was either sinus or follicular in type, or of both types. A less constant feature was infiltration by eosinophil granulocytes and plasma cells. Foam cells containing sudanophilic fat were found in moderate numbers in 7 out of 12 specimens examined in frozen section, while intracellular melanin pigment was present in most of the specimens. A control group of lymph nodes obtained from 7 patients with an itching rash but no exfoliation showed only one consistent difference—namely, the absence of reticulum-cell hyperplasia.

The authors point out that the importance of the syndrome of exfoliation with lymph-node enlargement is that unfamiliarity with its manifestations may occasionally lead to confusion of the histological appearance seen in these lymph nodes with that of some grave reticulosis. In discussing incidence the authors suggest that the 13 cases described probably represent the sum total of such cases occurring in 4 years among a population of nearly 500,000. *S. T. Anning*

821. **Some Observations on the Nature, Origin and Possible Functions of the Squalene and other Hydrocarbons of Human Sebum**
B. BOUGHTON, I. S. HODGSON-JONES, R. M. B. MACKENNA, V. R. WHEATLEY, and A. WORMALL. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **24**, 179–189, March, 1955. 3 figs., 27 refs.

In an earlier study (MacKenna *et al.*, *J. invest. Derm.*, 1950, **15**, 33; *Abstracts of World Medicine*, 1951, **9**, 118) it was found that human sebum contained hydrocarbons in the proportion of about one-sixth of the total weight, and that squalene was a major constituent, accounting for about one-third of the hydrocarbons. This substance is possibly an intermediary in the metabolism of cholesterol, although its precise relationship to that process is not yet known. In further experiments carried out at St. Bartholomew's Hospital, London, pooled batches of sebum extracted from the skin of the forearms of groups of healthy students showed wide variations in hydrocarbon content, as also did different samples from the same subject on different days and from different areas. Estimations of the squalene content of the sebum at different ages showed it to be much lower in children than in adults, but there was no significant difference between sebum from adult males and females. In three women daily estimations were carried out to determine whether there were any variations in the squalene content of sebum associated with the menstrual cycle. In one case there was a marked fall during menstruation, but this was not observed in the other two subjects. No significant differences in the squalene content of the sebum were observed between 20 normal individuals, 20 patients with seborrhoeic dermatitis, and 20 patients with psoriasis. The feeding of squalene or cholesterol to 3 normal males did not cause any alteration in the squalene content of the sebum, and the local application of squalene to 13 patients with a variety of skin diseases and to normal controls appeared to have no effect whatever. It is possible that the excretion of squalene in the human sebum represents the elimination of a metabolically useless substance, possibly formed in excess in connexion with the biosynthesis of cholesterol. The wide daily variations in the squalene content of sebum and the differences between sebum from various skin areas of the same subject indicate that the composition of the surface film of fat is not static, and this fact should be taken into consideration when comparisons are being made between normal subjects and those with skin diseases.
G. W. Csonka

822. **Melanin Formation in Vitiliginous Skin under the Influence of External Applications of 8-Methoxypsoralen**
N. B. KANOF. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **24**, 5–10, Jan., 1955. 11 refs.

8-Methoxypsoralen or "ammoidin" is regarded as the most important of the extracts of *Ammi majus* used in the treatment of vitiligo. In this paper from New York University the author reports the results obtained in treatment with this compound applied externally and in combination with ultraviolet irradiation. A total of 85 patients with vitiligo were treated, and where possible the effect on symmetrical lesions of a combination of 8-methoxypsoralen with subsequent ultraviolet irradiation or natural sunlight was compared with that of irradiation alone. The effects of a mixture of 8-methoxypsoralen and 8-*iso*amyleneoxypsoralen, another product of *Ammi majus*, were also observed.

Of the 85 patients, 32 showed formation of new pigment, but in only 6 could the repigmentation be regarded as cosmetically acceptable. The agent was equally effective when applied as a lotion or in a stearic acid cream base. No melanin formation was observed in areas treated by irradiation alone or with 8-methoxypsoralen alone without subsequent irradiation. Untoward re-

actions such as erythema, pruritus, exfoliation, bulla formation, and oedema occurred in 34 (40%) of the patients, severe reactions usually being the result of uncontrolled solar exposure. Natural sunlight was more effective in producing melanin than artificial ultraviolet light, but the results obtained with 8-methoxypsoralen alone were identical with those produced by a mixture of this substance with 8-*iso*amyleneoxypsoralen. Melanogenesis was usually most active in patients who first showed some degree of dermatitis, but was occasionally seen in subjects who showed little erythema.

Benjamin Schwartz

823. **Syringadenoma Papilliferum Lesions with and without Naevus Sebaceus and Basal Cell Carcinoma**
E. B. HELWIG and V. C. HACKNEY. *Archives of Dermatology* [*Arch. Derm. (Chicago)*] **71**, 361–372, March, 1955. 6 figs., 23 refs.

A series of 100 cases of superficial hidradenoma [by far the largest yet published] is reported from the Armed Forces Institute of Pathology, Washington, D.C. As usual in a series from this source the majority of the patients were males (91) and this factor invalidates some of the figures. In 45 of the cases the lesions were present at birth. Over half the specimens (55) were from the scalp, 21 from other parts of the head and neck, 2 from the perineum, and one from the scrotum; none came from the axilla. In no case was the lesion malignant. In 34 cases sebaceous glands of the epidermis were sufficiently increased in number and size as to suggest naevus sebaceus. In 9 cases a rodent ulcer (or at least rodent-ulcer-like proliferation of the epithelium) was seen near the hidradenomata.

The authors consider the lesion to be a true tumour of the sweat-gland ducts, arising from the ducts of eccrine glands or, more probably, from a gland intermediate between eccrine and apocrine.

Bernard Lennox

DERMATOSES

824. **A Therapeutic Assay of Topically Applied 9-α-Fluorhydrocortisone Acetate in Selected Dermatoses**
V. H. WITTEN, M. B. SULZBERGER, E. H. ZIMMERMAN, and A. J. SHAPIRO. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **24**, 1–4, Jan., 1955. 8 refs.

The replacement of the 9-α hydrogen atom in cortisone and hydrocortisone by a halogen has been shown to enhance the glucocorticoid activity of these substances when administered systemically. In the study here reported the clinical effect of such a derivative of hydrocortisone applied topically was compared with that of hydrocortisone free alcohol. Concentrations of 0·5, 0·2, and 0·1% of fluorohydrocortisone acetate and hydrocortisone free alcohol were incorporated in either a lotion or a "plasticized petrolatum base" and applied to the skin of 62 patients suffering from dermatoses previously reported to be amenable to treatment with topical hydrocortisone, such as atopic dermatitis, contact dermatitis, nummular eczema, and lichen simplex chronicus.

Comparison of simultaneously treated, symmetrically situated lesions was possible in 51 cases, and from the tabulated results it is seen that in 28 of these the area treated with fluorohydrocortisone showed better results than that treated with hydrocortisone free alcohol, in 8 cases the difference being very marked. In 16 cases the two compounds were equally effective, in 6 the fluorohydrocortisone was less effective, while in 2 cases both were ineffective. There did not seem to be any significant difference in effect between the lotion and the ointment. No systematic study of the comparative efficacy of the various concentrations was made, but the authors had the impression that the 0·2% concentration was in general more effective than the 0·1%. There were no instances of allergic sensitization or of local or of systemic damage resulting from the use of either preparation during the period of observation.

The authors conclude that 9-α-fluorohydrocortisone is slightly more effective than the hydrocortisone free alcohol in the topical treatment of the selected dermatoses treated.

Benjamin Schwartz

825. **Besnier's Prurigo: Observations on Abnormal Cutaneous and Central Nervous Reactions**
B. RUSSELL and S. L. LAST. *British Journal of Dermatology* [*Brit. J. Derm.*] **67**, 65–72, Feb., 1955. 23 refs.

The authors, from the London Hospital, present the results of a study of the reactivity of the skin and of the central nervous system in Besnier's prurigo, based on their own experience combined with a review of the literature. They find that in this disease firm stroking of normal areas of skin gives rise to the normal red line with a conspicuous white *tache* on each side of it. In areas affected by prurigo the only change is blanching along the line of stroking. This white dermatographism is unaffected by cold, heat, local analgesia, or sympathetic block, or by local intradermal injection of antagonists to cholinesterase, acetylcholine, histamine, and adrenaline. On the other hand it is abolished by the intracutaneous injection of Compound 48-80, which is a very potent liberator of histamine. The cause of the white dermatographism seems to be an abnormal tonicity of the cutaneous blood vessels, this tonicity being independent of the peripheral nerve supply and of stimuli from the central nervous system. Electroencephalographic studies have shown a significantly higher incidence of abnormal tracings in patients with Besnier's prurigo than in the general population. The authors consider it probable that the fundamental pathological change in this disease pervades the whole ectoderm. In their opinion the importance of seasonal and climatic factors has been exaggerated.

E. Lipman Cohen

826. **Besnier's Prurigo: an Ectodermal Defect**
J. T. INGRAM. *British Journal of Dermatology* [*Brit. J. Derm.*] **67**, 43–49, Feb., 1955. 11 refs.

In describing Besnier's prurigo the author emphasizes that the disease is not an eczema. It usually appears in infancy or early life, and when it is fully established the whole epidermis is thickened and has a dirty, earthen hue. There is often xerodermia, and abnormal pigmentation

which may be diffuse or patchy. It is due to an inborn epidermal abnormality. Seasonal variation may be pronounced. When severe the condition is incurable, but remissions occur in mild cases. Cataract develops in about 20% of patients during adolescence or early adult life. Victims of the disease are essentially individualists, the accompanying nervous and emotional instability probably being due to involvement of the central nervous system. The eczema and asthma which usually occur are secondary manifestations, so that the primary prurigo should not be regarded as an allergic disease; neither should it be considered as having a psychological basis. Males are affected more often than females, and a positive family history is obtainable in about two-thirds of the cases.

In discussing management the great importance of adjustment to climatic factors is stressed. Many patients seem to prefer a warm, dry climate, but the author states that those who do not sweat are usually more comfortable in cold weather. The fact that the parents often have the same temperament as an affected child and are over-anxious and over-possessive sometimes makes it advisable to move the patient from the atmosphere of his own home to a different—and "indifferent"—environment. ACTH and cortisone are useful in treating the secondary manifestations and in helping to control the itching of Besnier's prurigo, but they do not affect the primary disease. Hydrocortisone ointment is helpful in treating eczematization of the eyelids, face, and neck. Antihistamines are condemned by the author as useless both internally and externally.

E. Lipman Cohen

827. **Aplastic Anaemia following Mepacrine Treatment of Lupus Erythematosus**

M. D. PATON, M. J. RIDDELL, and J. A. STRONG. *Lancet* [*Lancet*] **1**, 281–282, Feb. 5, 1955. 11 refs.

828. **The Visceral Lesions of Pemphigus.** (Les lésions viscérales du pemphigus)

J. CHARPY, G. TRAMIER, and A. STAHL. *Presse médicale* [*Presse méd.*] **63**, 436–440, March 23, 1955. 12 figs., 12 refs.

The authors consider, from their experience at the Dermatological Clinic of the University of Marseilles, that the visceral lesions of pemphigus form an integral part of the disease. They present 3 cases studied in great detail clinically and histologically, necropsy being performed within 4 hours of death. The relevant literature is reviewed, and the necropsy findings in the present cases described and compared with those of Bolgert and of Richter.

Fatty degeneration in the liver and discrete infiltration of the portal tracts were constantly present; a peculiar vacuolization of the nuclei of the liver cells was noted which gave a positive McManus reaction and was regarded as due to the presence of glycogen.

The spleen showed capsular thickening, increase in interstitial fibrous tissue, and increased density of collagen. The kidneys were involved in all 3 cases, and here, too, McManus's stain demonstrated the presence of glucoprotein material lying between the loops of the glomerular tuft and in the lumen of tubules as hyaline casts.

Myocardial necrosis was present, with Zenker's hyaline degeneration and narrowing of the arteriolar lumen by deposits of a hyaline, McManus-positive material in the wall in all cases.

The adrenal medulla had undergone almost complete autolysis (in spite of the prompt necropsy) and the cortex showed degenerative changes.

In all the parenchymatous organs unusually dense connective-tissue capsules and trabeculae were found, together with widespread arteriolar changes—namely, deposits of a McManus-positive material in the vessel wall, occasionally occluding the lumen; in these vascular changes pemphigus closely resembled disseminated lupus erythematosus (as also in inversion of the serum albumin: globulin ratio and the hypoproteinaemia).

In the lungs it was difficult to distinguish between primary lesions and those due to superimposed infection.

Only in one case was part of the central nervous system examined, and here degeneration of posterior root ganglion cells was demonstrable.

In conclusion it is pointed out that the significance of the adrenal changes is difficult to evaluate because most of these patients had had substitution therapy with pituitary or adrenal hormones or both. The hepatic and renal changes and those in the ground substance of connective tissue on the other hand are undoubtedly significant, and the pathogenesis of pemphigus in relation to these and the other findings is discussed.

F. Hillman

829. **"Pemphigoid" (Para-pemphigus): Its Relationship to other Bullous Dermatoses**

J. R. PRAKKEN and M. J. WOERDEMAN. *British Journal of Dermatology* [*Brit. J. Derm.*] **67**, 92–97, March, 1955. 2 figs., 12 refs.

Of a series of 66 bullous eruptions seen in the Dermatological Department of the University of Amsterdam since 1947, 11 were considered to be due to pemphigus vulgaris, 19 to pemphigoid (although the differentiation from pemphigus vulgaris could not be made with certainty in 4), 21 to dermatitis herpetiformis, and 9 to other conditions. (The term "para-pemphigus" is preferred by the authors to "pemphigoid" and "bullous pemphigoid" for the description of a bullous dermatosis which clinically resembles pemphigus vulgaris and is characterized histologically by subepidermal bullae without acantholysis, as is seen in Duhring's dermatitis herpetiformis.)

In 7 of the 19 patients with pemphigoid the eruption was localized to one region at first for 1 to 18 months. Three of the patients were children aged 2 to 4 years at the time of onset. All the patients have been observed for a year or more following treatment, and 3 have died (at 68, 74, and 84 years of age respectively). Cortisone and ACTH (corticotrophin) were employed in the treatment of 11 cases, including the 3 fatal cases. The response was favourable in the 8 others.

R. R. Willcox

Paediatrics

830. **Honey in Infant Feeding**
A. J. VIGNEC and J. F. JULIA. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **88**, 443–451, Oct., 1954. 2 figs., 10 refs.

A light processed clover honey added to the feed of evaporated cow's milk was given to 136 infants at the New York Foundling Hospital and the rate of growth and haemoglobin values were recorded. Two-thirds of the infants were under one month old when first seen, and the period of observation in most cases was 4 weeks or longer. Two control groups received sugar in the form of " dextrimaltose " and " karo " respectively.

Only 2 of the infants receiving honey required treatment for anaemia; the incidence of anaemia was higher in the control groups, the difference being " probably significant ". In other respects the progress of the infants given honey was equal but not superior to that of the group given dextrimaltose. The results obtained with honey, as judged by gain in weight, linear growth, and haemoglobin value, were slightly better than those obtained with karo. The honey was also more readily accepted and was well tolerated. The authors conclude that honey " has a definite place in infant feeding ". [Apart from emphasizing its palatability, however, they make no recommendations concerning the circumstances in which it should be used.] *Mark S. Fraser*

THE NEWBORN INFANT

831. **Radioactive Iodide Uptake of Normal Newborn Infants**
L. VAN MIDDLESWORTH. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **88**, 439–442, Oct., 1954. 7 refs.

In this study, carried out at the John Gaston Hospital, Memphis, Tennessee, radioactive iodide was administered intramuscularly to 7 healthy male infants on the 3rd day of life in a single dose not exceeding 1·5 microcuries. The uptake of ^{131}I by the thyroid gland was measured 24 hours later. In 6 of the infants it exceeded 60% of the test dose, in 2 cases being greater than 90%. The normal uptake in the newborn infant is therefore high, with a range of values which in adult life would indicate hyperthyroidism. *Mark S. Fraser*

832. **Exchange Transfusion in Haemolytic Disease of the Newborn**
W. WALKER and G. A. NELIGAN. *British Medical Journal* [*Brit. med. J.*] **1**, 681–691, March 19, 1955. 4 figs., 32 refs.

Experience of exchange transfusion in 250 consecutive cases of haemolytic disease of the newborn seen between March, 1947, and March, 1954, is described in this paper from the University of Durham. A steady improvement in results over this period (the mortality in the years 1952 and 1953 was only 2%) is ascribed to increased familiarity with the technique and more precise selection at an early stage of infants likely to require treatment. In the light of experience the criteria determining the need for transfusion were changed on two occasions. Since September, 1951, the criteria have been a cord-blood haemoglobin level of 14·8 g. per 100 ml. or less and a cord-blood haemoglobin level between 14·8 and 17·7 g. per 100 ml. when the cord-blood bilirubin level is 2·8 mg. per 100 ml. or more. From the authors' results the risk of kernicterus appears to be negligible if an exchange transfusion of at least 80 ml. per lb. (176 ml. per kg.) body weight is given within 9 hours of birth to infants selected according to the above criteria. The only 2 deaths from kernicterus in the later series occurred in premature infants, and the authors emphasize that exchange transfusion in prematurity should be avoided whenever possible.

The technique and apparatus are clearly and carefully described, and the complications and hazards are fully discussed. [This is a most useful appraisal of the subject.] *Margaret D. Baber*

833. **Rupture of the Spleen. A Complication of Erythroblastosis Fetalis**
H. F. PHILIPSBORN, H. S. TRAISMAN, and D. GREER. *New England Journal of Medicine* [*New Engl. J. Med.*] **252**, 159–162, Feb. 3, 1955. 3 refs.

Four fatal cases of rupture of the spleen as a complication of erythroblastosis foetalis are reported from the Children's Memorial Hospital, Chicago. In 3 of the infants exchange transfusion had been completed, but in the fourth death occurred before treatment had been instituted. In no instance could the cause of death be assigned with certainty to rupture of the spleen alone. Possible predisposing factors contributing to this complication include extramedullary haematopoiesis, increased phagocytosis, weakening of the supportive structure of the spleen, increased intra-abdominal pressure, " damming back " of blood from the liver, increased blood volume, displacement of the spleen by an enlarged liver, and a haemorrhagic tendency. These potential pathogenetic factors are discussed, and the authors conclude that those most likely to cause splenic rupture in erythroblastosis foetalis are extramedullary haematopoiesis, increased phagocytosis, weakening of the supportive structures of the spleen, and a tendency to haemorrhage. *Jas. M. Smellie*

834. **The Management of Congenital Oesophageal Atresia and Tracheo-oesophageal Fistula**
K. D. ROBERTS, I. J. CARRE, and J. M. INGLIS. *Thorax* [*Thorax*] **10**, 45–52, March, 1955. 4 figs., 6 refs.

The authors of this paper from the Children's Hospital, Birmingham, briefly discuss the history of the surgical treatment of congenital tracheo-oesophageal fistula and

the diagnosis of this condition. They describe their preoperative preparation of the patient and point out that since the infant is generally only one to 2 days old correction of dehydration is rarely necessary. Some details of operative technique are given, the authors emphasizing that the most important factor is to secure an anastomosis which is not under tension. Simple ligation of the fistula should be avoided and a more formal repair of the trachea performed. A single layer of interrupted sutures is used for the anastomosis. Recently the authors have performed gastrostomy on the first or second postoperative day and now recommend this as a routine procedure. The feeding of the infant in the early postoperative period is discussed at some length, with details of the formulae which have been found satisfactory. The complications and their treatment are described. Of 14 infants operated on in a recent 12-month period, 8 survived. *J. R. Belcher*

835. **Peritonitis in the Neonatal Period**
P. P. RICKHAM. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **30**, 23–31, Feb., 1955. 10 figs., bibliography.

Whereas peritonitis was formerly regarded as rare in the newborn, many cases have been reported in the literature during the last 5 years. Among approximately 250 admissions to the Neonatal Surgical Unit at Alder Hey Children's Hospital, Liverpool, during a period of 3½ years there were 17 cases of peritonitis, representing about 7% of all urgent admissions and 17% of all cases of neonatal intestinal obstruction.

Meconium peritonitis accounted for 7 of these cases, and the author emphasizes that only cases of purely chemical peritonitis should be included in this category, cases in which abnormal communication between bowel and peritoneum persists after birth soon becoming contaminated and indistinguishable from bacterial peritonitis. There are two types of case, those with mechanical intestinal obstruction, from such causes as atresia, stenosis, volvulus, and bands, and those without. In the second type the occurrence of perforation is difficult to understand. Aplasia of the muscularis mucosae, vascular insufficiency, and hypertrophy of the crypts of Lieberkühn have been suggested as possible causes. In 6 of the author's cases no perforation could be found; in one case, however, there were ulcers involving the muscular coat of the intestine, and in another the muscle layers were incomplete and contained giant cells and calcified meconium, and it must be assumed in such cases that perforations were present and had subsequently healed. Trauma as a cause of perforation is unlikely.

The remaining 10 cases were of acute bacterial peritonitis in which a gastro-intestinal perforation had occurred during or after birth and in which meconium was not found in the peritoneal cavity. In 4 cases an abscess in the right iliac fossa was drained without a perforation being seen. In the remaining 6, perforations were found, the sites including the stomach, a volvulus, a Meckel's diverticulum, a duplicated ileum, and the terminal ileum (2 cases). The case of gastric perforation followed a difficult breech delivery; at operation a large rent was found in the lesser curve, which was sutured, but the patient died. Necropsy showed extradural haemorrhage, thrombosis of the inferior vena cava, and infarction of the stomach and other viscera. The majority of cases of bacterial peritonitis, however, are due to perforation of the small or large bowel, which has a poor muscular coat at birth.

The clinical picture of neonatal peritonitis is one of intestinal obstruction, present at birth in cases of atresia, developing later in cases of stenosis. The presence of shock indicates a recent perforation. Distension was a common feature in the author's cases, and sometimes visible peristalsis, oedema in the flanks, and absence of liver dullness occurred. Blood and mucus were present in the stools in the cases of abscess formation, and pneumoperitoneum and occasionally calcified meconium were seen on *x*-ray examination.

There were 7 deaths in this series, a mortality of 41·2% compared with 19·8% in 81 cases of obstruction without peritonitis. The cause of death was bronchopneumonia in 3 cases, and gastroenteritis, toxaemia, thrombosis of the inferior vena cava, and intestinal fistula respectively in the remaining 4 cases. *Charles Nicholas*

836. **Staphylococcal Infection in the Newborn Treated with Erythromycin**
J. O. FORFAR, A. F. MACCABE, C. L. BALF, H. A. WRIGHT, and J. C. GOULD. *Lancet* [*Lancet*] **1**, 584–587, March 19, 1955. 15 refs.

The value of erythromycin in treating neonatal staphylococcal infections was investigated over a period of 9 months in the maternity units (E and W) attached to two general hospitals in Edinburgh. In Unit E, of 140 infants with staphylococcal infection, 89 had conjunctivitis, 19 skin pustules, 13 infection of the umbilicus, and 9 local cellulitis; the condition in the remaining 10 is not specified. Erythromycin was given by mouth in a dosage of 20 mg. per lb. (44 mg. per kg.) body weight daily in fractionated doses 6-hourly for an average of 3½ days (range 2 to 8 days), the treatment being stopped when clinical cure was established. In Unit W 112 infants were infected, 68 having conjunctivitis, 27 skin pustules, 4 umbilical sepsis, and 13 cellulitis. Only 80 of these infants were treated, erythromycin being given by mouth in the same dosage as in Unit E for an average of 4½ days (range 2 to 9 days); in addition they received a daily injection of 0·125 g. of streptomycin. In both units erythromycin was taken readily; vomiting was rarely encountered and diarrhoea was not observed. In no case did clinical thrush develop and the drug did not appear to alter the bacterial flora of the faeces. The staphylococci isolated were all sensitive to erythromycin, many were resistant to penicillin, and a smaller number were resistant to streptomycin. When the nasal flora of members of the staff of the maternity units was examined 70% of the staff in Unit E and 38% in Unit W were found to be carriers of *Staph. pyogenes*. Phage-typing showed the organisms to be of 4 main types in both staff and patients, indicating that cross-infection was common. From the infants given

streptomycin an increasing number of streptomycin-resistant staphylococci were isolated. Contrary to experience in some other units, strains of staphylococci resistant to erythromycin did not emerge during the 9 months of this investigation. *R. M. Todd*

837. **Clinical Picture of Severe Generalized Viral Infection in the Newborn**
J. H. COLEBATCH. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 377–382, March 12, 1955. 19 refs.

In this paper from the Royal Children's and Royal Women's Hospitals, Melbourne, the clinical features of two similar neonatal infections—generalized cytomegalic inclusion disease and herpes simplex viraemia—are described with reference to cases seen in recent years in Australia. Either of these two conditions may be the cause of stillbirth and their presence should be suspected in cases in which deepening jaundice and haemorrhages occur during the first week of life. Cytomegalic inclusion disease may occur as an intra-uterine infection. It may resemble erythroblastosis, but the reaction to the Coombs test is negative. Characteristic intracytoplasmic and intranuclear inclusion bodies are found in the enlarged cells of most organs. Herpes simplex viraemia may present as an infective hepatitis during the first week of life or as encephalitis in the second. Characteristic intranuclear inclusion bodies are found in the liver, the virus being isolated from this organ. Premature infants are particularly susceptible to these severe neonatal virus infections. *D. Geraint James*

See also Pathology, Abstract 621, and Haematology, Abstracts 740–41.

CLINICAL PAEDIATRICS

838. **High Plasma Calcium and Influencing Factors in Interstitial Plasma Cell Pneumonia in Infants.** [In English]
N. HALLMAN, H. TÄHKÄ, and E. K. AHVENAINEN. *Annales paediatriae Fenniae* [*Ann. Paediat. Fenn.*] **1**, 34–49, 1954–55. 5 figs., 27 refs.

The authors studied the blood chemistry in 59 cases of interstitial plasma-cell pneumonia in premature and full-term infants at three Helsinki hospitals during the period 1950–4. In almost every case the plasma calcium level was found to be increased, in some to more than 15 mg. per 100 ml. Although high doses of vitamin D were given to all these babies as a prophylactic measure against rickets and may have contributed to it, the hypercalcaemia did not appear to be simply a result of hypervitaminosis D: premature infants without pneumonia who received the same dosage of vitamin D had no corresponding hypercalcaemia, and there was often a rapid fall in the plasma calcium level in infants recovering from pneumonia. The alkali reserve and the chloride and alkaline-phosphatase levels in the blood were normal in all cases of interstitial pneumonia, the only other abnormality found in the plasma being an increase in the non-protein nitrogen content. There was no correlation between the degree of hypercalcaemia and prognosis.

The blood chemistry in these cases is compared with that in idiopathic hypercalcaemia, and it is suggested that the latter may also be caused by some infection. The possibility that anoxaemia plays some part in the increase in plasma calcium level in interstitial plasma-cell pneumonia is discussed. *H. S. Baar*

839. ***Pneumocystis* Pneumonia and its Relation to Interstitial Plasma-cell Pneumonia.** (La pneumonie à *Pneumocystis*: ses rapports avec la pneumonie interstitielle à plasmocytes)
LE TAN VINH. *Archives françaises de pédiatrie* [*Arch. franç. Pédiat.*] **11**, 1035–1054, 1954. 21 figs., 10 refs.

The author has applied the silver impregnation method of Del Rio Hortega to the study of *Pneumocystis carinii* in sections of lung tissue from cases of interstitial plasma-cell pneumonia. While excellent results were obtained, both with and without preliminary oxidation with permanganate, with frozen sections, the results with paraffin sections were somewhat irregular and less satisfactory. [The photomicrographs illustrating the findings are excellent.] There follows a description of 3 typical cases of *Pneumocystis* pneumonia and one particularly interesting atypical case. This last was in an infant aged 27 months at the time of death who had a history of eczema and cervical adenitis before developing *Pneumocystis* pneumonia. The lungs showed the typical honeycomb appearance with *Pneumocystis* present in large numbers in the alveoli, but contrary to the usual finding infiltration of the interalveolar septa was absent or minimal. The author suggests that the intra-alveolar exudate is the primary and characteristic change in *Pneumocystis* pneumonia, and that the reaction of the interstitial tissue is secondary, its extent depending on such factors as the degree of immaturity of the affected tissue. *H. S. Baar*

840. **Coeliac Disease. Results of Late Treatment with Gluten-free Wheat Diet**
J. W. GERRARD, C. A. C. ROSS, and J. M. SMELLIE. *Lancet* [*Lancet*] **1**, 587–589, March 19, 1955. 1 fig., 8 refs.

The response to a gluten-free wheat diet of 18 patients at the Children's Hospital, Birmingham, who had had coeliac disease for 3 to 14 years is reported. The patients, who were 4 to 16 years of age, were losing an average of 8·3 g. of fat daily in the stools. The height and weight of the children were measured and the fat content of the faeces was estimated over a period of 5 days before treatment started, these values being again determined after the diet had been given for at least 4 months, the duration of treatment ranging from 4 to 25 months. A sudden improvement in the height and weight gradients was noticed, the gain in weight being 2½ times and the increase in height twice the pretreatment values. The mean daily faecal output of fat fell from 8·3 to 3·4 g., a figure which compared favourably with an average daily fat excretion of 2·7 g. in 20 healthy children. It was also observed that growth of hair and

nails was more rapid and that vitality improved. These results support the contention that a gluten-free diet is beneficial not only in the acute phase of coeliac disease but also in the latent or quiescent phase seen in later childhood and adolescence. *R. M. Todd*

841. **Congenitally Short Frenula of Upper Lip and Tongue**

M. C. OLDFIELD. *Lancet* [*Lancet*] **1**, 528–530, March 12, 1955. 6 figs.

The author, from St. James's Hospital, Leeds, describes the technique of operation to correct three congenital abnormalities of the upper lip and tongue: (1) short frenulum linguae, (2) short frenulum of the upper lip, and (3) prolapsing mucosa of the upper lip. He considers that operation is necessary for short frenulum linguae because it may be responsible for difficulty in the pronunciation of certain consonants. The frenulum is divided transversely and the wound closed longitudinally with interrupted chromic catgut sutures. The procedure is similar for short frenulum of the upper lip, except that it is necessary also to remove the prolongation of the frenulum which extends between the two central incisors down to the bone, a small periosteal elevator being used to roughen the bone. Unless this deformity is corrected it gives rise to the unsightly abnormality of a large gap between the central incisors. In prolapsing mucosa of the upper lip—an uncommon condition—the lining mucosa dips below the vermilion border of the lip. An ellipse of the abnormal mucosa is excised in a horizontal direction and the wound closed with " end-on " mattress stitches of chromic catgut, the deep bite of the stitch picking up the orbicularis oris muscle and the more superficial bite the mucosa. The author states that this last condition " has not yet received an official name " and that the term " congenital prolapsing mucosa of the upper lip ", though cumbersome, describes it best. *Charles Nicholas*

842. **The Cardio-oesophageal Syndrome in Childhood**

I. FORSHALL. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **30**, 46–54, Feb., 1955. 10 figs., 15 refs.

A series of 93 cases of incompetence of the cardia in children is reported from the Alder Hey Children's Hospital, Liverpool. They are divided into two groups, in one of which the cardia was normal in position and the condition was one of " lax oesophagus ", whereas in the other the cardia was above the diaphragm, the condition being one of sliding hiatal hernia.

The cases of lax oesophagus numbered 58. Vomiting, projectile in 43% of cases, dated from birth, with haematemesis in 26% and loss of weight in 23%. Visible peristalsis occurred in 19% and there was an associated pyloric stenosis in 6 cases. The author suggests that the vomiting in this type of case may be due to hypertonicity of the alimentary tract below the cardia. This would also explain the high incidence of pyloric stenosis and the gross dilatation of the oesophagus which was uniformly present despite the lack of obstruction at the cardia. It is also of interest to note that one infant developed jaundice due to spasm of Oddi's sphincter. Radiological examination in cases of lax oesophagus shows free regurgitation, dilatation of the lower oesophagus, patency of the cardia, increase in the angle between stomach and oesophagus, and hyperperistalsis. Oesophagoscopy shows a voluminous oesophagus containing gastric contents, and oesophagitis is often present. The cardia is recognizable and is normally placed. At necropsy in 3 cases it was shown that the cardia was patulous and could not be drawn up into the chest. Medical treatment is all that is required as a rule. The infant is kept upright by means of pillows, a harness, or other device and small, thickened feeds are given; antacids and " pylostropin " (atropine methonitrate) are of some use. Such measures were successful in 79% of cases. In one case, after repeated relapses, the oesophageal hiatus was narrowed by suture with good effect, while 4 children later developed short oesophagus from contracture following severe oesophagitis. There were 7 deaths in this group, the causes being gastroenteritis, necrosis of the lower oesophagus, septicaemia, haematemesis, lung abscess, and inhalation of vomit respectively in 6 cases, the remaining child dying on induction of anaesthesia for oesophagoscopy.

Sliding hiatal hernia, which occurred in 35 cases, is probably caused by a poorly developed diaphragmatic hiatus combined with oesophagitis and spasm or with disproportion in growth between the child and his oesophagus. That part of the stomach which is lying above the diaphragm can be recognized from the appearance of the mucosa at the lower end of the oesophagus on oesophagoscopy and radiography. The oesophagus is not dilated unless there is a stricture below. Symptoms are absent unless the cardia is incompetent. Haematemesis is more common and projectile vomiting less common than with lax oesophagus, and visible peristalsis does not occur unless pyloric stenosis is also present. There is a greater tendency to oesophagitis and rapid shortening in this group, and in 30% of the author's cases peptic ulcers occurred within an inch (2·5 cm.) of the cardia, one of which perforated the mediastinum, while strictures also occurred in 30% of cases and were more common in those with ulcers, but were difficult to visualize radiographically. The symptoms, consisting in dysphagia, retrosternal and posterior thoracic pain, and regurgitation of meals, are temporarily relieved by instrumental dilatation, but in general cases of sliding hiatal hernia do not respond permanently to medical treatment. Failure to gain weight, persistent severe oesophagitis, ulceration, and strictures are absolute indications for operation, which was carried out in 30 cases in the present series. Thoracotomy and exposure of the stomach through the diaphragm is the best approach, success depending on adequate oesophageal mobilization to the level of the aortic arch, complete separation of the stomach from the diaphragmatic hiatus, and its careful fixation below the diaphragm by sutures. There was one postoperative death, the condition of the remaining 29 patients having been completely relieved, although in 4 cases a second operation was necessary owing to recurrence after a first attempt in which the stomach was not exposed.

Charles Nicholas

843. **Intestinal Obstruction by Duodenal Diaphragm**
A. F. FERGUSON and N. J. ROTHFIELD. *Great Ormond Street Journal* [*Gt Ormond Str. J.*] No. 8, 105–112, 1954–5. 5 figs., 7 refs.

844. **Congenital Defects in the Pelvic Parasympathetic System**
O. SWENSON. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **30**, 1–7, Feb., 1955. 4 figs., 10 refs.

Having noted that although transverse colostomy relieved the symptoms of congenital megacolon (Hirschsprung's disease) completely, the symptoms invariably recurred in such cases on subsequent closure of the colostomy, the author concluded that a functional obstruction must be present in the colon in this disease. Further investigations showed that a segment of the rectosigmoid colon without peristaltic activity was constantly present in cases of Hirschsprung's disease, and a technique was evolved for the resection of this inactive segment with restoration of continuity. This operation has been performed by the author in 150 cases during the past 9 years at the Boston Floating Hospital (Tufts College Medical School), the rectum and sigmoid being excised and anastomosis being carried out 1½ cm. from the anal mucocutaneous junction. Ganglion cells were absent from the wall of the excised bowel segment as far down as the internal sphincter in all the author's cases except one in which there was a cuff of distal rectum 4 to 6 cm. long containing normal ganglion cells, but with an aganglionic segment proximal to this. It is therefore concluded that Hirschsprung's disease is due to a congenital malformation of the pelvic parasympathetic system.

The symptoms of Hirschsprung's disease date from birth, whereas those of habit constipation, with which it might be confused, start at 2 to 3 years of age. Moreover, in the former condition the faeces are impacted in the sigmoid colon and none can be felt in the rectum. The diagnosis can usually be made unequivocally on barium-enema *x*-ray examination, but may be difficult in the first 8 months of life and in children on whom colostomy has already been performed. The author has therefore developed a biopsy technique whereby a triangular piece of rectal wall measuring about 1 × ½ cm. can be removed per anum from just above the internal sphincter for histological examination. This procedure has been carried out in 40 cases without complications: 19 of the specimens were aganglionic and in all these cases the patient proved to have Hirschsprung's disease when operated upon, whereas the remaining 21 showed normal ganglion cells and in each of these cases the history and *x*-ray appearances were characteristic of chronic constipation.

The author carries out resection without preliminary colostomy in 75% of cases, colostomy being reserved for infants who are seriously ill. Among his 150 cases the following complications have arisen: leaking anastomosis (3 cases), stricture (6, of which 5 responded to dilatation), perirectal abscess (1), and recto-vaginal fistula (1). Faecal incontinence has not occurred as a result of the operation. There were 4 deaths among the 20 children operated on in the first 6 months of life, but only one death among the remaining 130 patients.

The pelvic parasympathetic system supplies the bladder as well as the rectum and lower colon, and megalo-bladder or megalo-ureter may occur in association with Hirschsprung's disease or alone. In megalo-bladder the bladder capacity is 2 or 3 times greater than normal and the pressure may rise to 25 or 35 cm. H_2O (normal 10 to 12 cm.). Such children void urine only once or twice daily, leaving a large residuum. In cases of megalo-bladder with a high intravesical pressure the ureters frequently become dilated, and in such cases ureteric peristalsis is present, though the rate is slower than normal, whereas it is absent in cases of megalo-ureter with a normal bladder. In the former type of case urethral catheterization, suprapubic cystostomy, or resection of the bladder neck reduces the amount of dilatation of the upper urinary tract and improves the child's health. In 8 cases of megalo-bladder examined post mortem by the author a reduction in the number of ganglion cells which are normally aggregated around the ureteric orifices in the bladder-wall was found. The author therefore concludes that, like Hirschsprung's disease, megalo-bladder and megalo-ureter are due to a congenital malformation of the pelvic autonomic system, and warns against operation on the lower end of the ureter in cases of megalo-ureter. He cites the cases of 2 children who had undergone resection and re-implantation of the ureters and who were subsequently unable to micturate, the defective innervation of the bladder having presumably been further damaged by the operation.

Charles Nicholas

845. **Incidence of Dyspepsia Coli (O—26; O—55; O—111) in Sporadic Infantile Gastroenteritis.** [In English]
N. HALLMAN, I. RANTASALO, L. TUUTERI, and M. KOTILAINEN. *Annales paediatriae Fenniae* [*Ann. Paediat. Fenn.*] **1**, 27–33, 1954–55. 16 refs.

846. **Nitrofurantoin Therapy of Urinary Tract Infections in Children**
S. H. JOHNSON and M. MARSHALL. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **89**, 199–201, Feb., 1955. 7 refs.

At the Children's and Western Pennsylvania Hospitals, Pittsburgh, 29 children with urinary infections were treated with nitrofurantoin. In 11 cases an anatomical abnormality of the urinary tract was present, and although the drug proved effective in reducing or controlling pyuria and fever in 5 of these, only in one was the urine rendered sterile. Of the 18 cases in which the urinary tract was normal, in 11 the urine became sterile (temporarily only in 4), and in 2 others fever and pyuria were controlled. The dosage used was 10 mg. per kg. body weight daily, divided in 4 doses, and the treatment was continued for several weeks.

The chief value of this new drug would appear to be its action on *Proteus vulgaris*, for in more than half of the cases of infection with this organism the urine became sterile.

Wilfrid Gaisford

Public Health

847. **The Social and Psychological Backgrounds of Tuberculous Children**
D. ROSENBLUTH and J. BOWLBY. *British Medical Journl* [*Brit. med. J.*] **1**, 946–949, April 16, 1955. 3 refs.

A study was made of the social and emotional problems arising from tuberculous illness in a family by following up children admitted between birth and 4 years of age to a Middlesex sanatorium from 1940 to 1948; 56 children, from 55 families, who had had uncomplicated primary tuberculosis were available for investigation. The economic circumstances of the 55 families were rated as " comfortable, 6; fairly adequate, 20; poor, 16; and economic hardship, 13 "; housing conditions were rated as " very good, 10; good, 24; poor, 15; and inadequate, 6 ". Illness in the family had caused disruption in 26 families (in 22 through the death of a parent, with tuberculosis as the cause in 19 instances); the source of the child's infection was believed to be parental in 29 cases.

In the course of the inquiry it became apparent that far-reaching and complex psychological reactions were aroused by the existence of tuberculosis in a member of a family. Conscious fear of it and its implications was widespread, and about 20% of the parents dealt with such anxiety by attempting to deny that there had been any tuberculous illness, such attempts leading to failure to take proper measures for prevention and treatment. The reaction of a further 20% was a constant hypochondriacal fear for the family's health. There was a general tendency to over-protectiveness towards the child who had been ill, often associated with a feeling of guilt and personal responsibility for the child's illness. Instances were noted of the fear that the child would be " branded for life " and of ostracism with resultant loneliness. The authors feel that the emotional and social problems of tuberculous families require to be further studied and their needs to be met for the sake of family and community. *F. T. H. Wood*

848. **The Cancer Patient: Delay in Seeking Advice**
J. AITKEN-SWAN and R. PATERSON. *British Medical Journal* [*Brit. med. J.*] **1**, 623–627, March 12, 1955. 3 refs.

A study, based on detailed interviewing of 314 patients with cancer of the breast, cervix uteri, skin, or mouth showed that approximately one-half delayed seeking advice for 3 months or more, and a quarter for a year or more, after first noticing symptoms. Most of the patients with breast cancer suspected they had cancer; patients with the other three types of cancer were, in the main, ignorant of the significance of their symptoms. There was greater delay among those who suspected cancer than among those who did not.

Two quite distinct processes operate to cause delay. 1. *Ignorance.*—Here, delay in seeking advice clearly reflects the patient's general attitude towards " doctoring " and has no special relationship to cancer as such. 2. *Fear* (of cancer).—This is clearly indicative that, in some degree at least, the patient really " knows " the probable nature of the disease. Such fear may trigger a reasonable response and make for " immediate " action. Much more often, in the group analysed, it inhibited rational action and was the underlying factor causing delay, although this was camouflaged behind a variety of more superficial ostensible reasons. Testing by the Wechsler–Bellevue intelligence scale indicated that there was no significant relationship between delay and intellectual level as measured by this test.

These distinct and mutually exclusive attitudes to the different diseases must be recognized in any schemes for public education in this field.—[Authors' summary.]

849. **Early Cancer Detection and Education: a Pilot Trial**
J. WALTER and E. C. ATKINSON. *British Medical Journal* [*Brit. med. J.*] **1**, 627–631, March 12, 1955. 20 refs.

This paper describes a survey in a general practice, in which clinical medical examination was offered to patients between the ages of 40 and 70 combined with instructional propaganda in early cancer symptoms. Four hundred and twenty-two women and 415 men responded, making acceptance rates of 55% and 58%. A follow-up examination on the women was also carried out, including a vaginal cytological smear, bringing the total of examinations to about 1,000. The findings are reported, with details of malignant and non-malignant lesions discovered.

Some of the arguments for and against such examinations and their possible value in cancer morbidity and mortality are discussed. The psychological and financial aspects are also touched on. It is concluded that further experimental trials on similar lines would be justified, and are necessary before any appraisal of their long-term value can be made.—[Authors' summary.]

850. **Impregnation of Handkerchiefs, Ultra-violet Lighting, and Other Control Methods in Prevention of Upper Respiratory Disease**
T. C. MACDONALD, J. D. TONKINSON, J. PORTERFIELD, and K. R. DUMBELL. *British Journal of Preventive and Social Medicine* [*Brit. J. prev. soc. Med.*] **9**, 33–38, Jan., 1955. 5 refs.

The authors report a series of five trials of various possible methods of reducing the spread and incidence of upper respiratory infections which they have carried out at an R.A.F. station in successive periods during the years 1950 to 1953. The subjects were young apprentices aged 15½ to 17 and numbered between 1,200 and 1,800 at different times; they were divided into fairly self-contained and separate units which were very similar in their characteristics and conditions of life and thus facilitated the setting up of experimental and control groups during the investigations. The experimental

measures used, either singly or in combination, were: (1) the use of handkerchiefs impregnated with octyl cresol or with glycollic acid; (2) ultraviolet irradiation of the air in the barrack rooms to reduce airborne infection; (3) oiling of floors and oil impregnation of bed-clothes and pyjamas to control dustborne infection; and (4) the use of screens of the ordinarly folding type between beds to prevent direct spread by droplet infection. Infections were classified as colds, influenza, or sore throat, as diagnosed by the unit medical officer, or as self-reported colds, which were notified to the leading apprentice in each barrack-room.

The impregnation of handkerchiefs with octyl cresol did not lower the incidence of upper respiratory disease; nor was the incidence lowered in a trial which combined ultraviolet irradiation of the barrack room, oiling of floors and pyjamas, bed screens, and handkerchiefs impregnated with octyl cresol. But the use of handkerchiefs impregnated with glycollic acid (which has certain drawbacks of its own), combined with the general measures, resulted in a somewhat lower incidence of the common cold. The results are thus somewhat inconclusive and further, more prolonged, trials are advocated.

J. Cauchi

851. **The Epidemiology of Poliomyelitis in Europe in 1952 and 1953.** (Zur Epidemiologie der Poliomyelitis in Europa in den Jahren 1952 and 1953)

F. JUNK. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **80**, 315–318, March 4, 1955. 3 figs.

Basing his comments upon the Epidemiological and Vital Statistics Report issued by the World Health Organization for 20 European countries during the years 1952 and 1953, the author divides the incidence of poliomyelitis into six grades. While Denmark was the most affected country in 1952, most other countries had more or less serious outbreaks. In 1953 the disease had a milder character and a lower incidence, except in Sweden where the numbers rose to the level of a pandemic of considerable proportions. The course of poliomyelitis epidemics and their regional distribution are discussed.

Franz Heimann

852. **The Transmission of Infectious Mononucleosis**

R. J. HOAGLAND. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **229**, 262–272, March, 1955. 29 refs.

The author reviews the evidence available concerning the transmission of infectious mononucleosis. As a result of personal observations in 74 cases of the disease among cadets at the U.S. Military Academy over a period of 6 years, he concludes that the disease is spread chiefly by " direct intimate oral contact ", as in kissing, or more rarely through the medium of drinking vessels recently used by infected persons. He discounts the possibility of airborne droplet spread because he has rarely known spread of the disease to occur between room-mates or in open hospital wards, where airborne cross-infection is likely to occur. Of his patients, 4 had stated that they had engaged in intimate kissing on only one occasion, 40 days or so before the onset of symptoms, and on this he bases the hypothesis that the incubation period must be of the same order. The seasonal prevalence noted by him in February and August is explained by the increased opportunities for " intimate oral contact " during the Christmas and summer vacations!

[This paper cannot be regarded as a serious contribution to our knowledge of the mode of transmission of infectious mononucleosis.] *I. M. Librach*

853. **Cowpox in Man and its Relationship with Milker's Nodules**

B. LAURANCE. *Lancet* [*Lancet*] **1**, 764–766, April 9, 1955. 4 figs., 12 refs.

A clinical account is given of a case of cowpox in a Gloucestershire farmer who had never been vaccinated against smallpox. A lesion developed on his hand 3 days after he had observed that vesicles, which later ulcerated, had appeared on the teats of his cows. None of the other persons on the farm, all of whom had been vaccinated in infancy, developed the disease. During the course of his illness there was a significant rise in titre of complement-fixing antibodies to both cowpox and vaccinia virus.

The author discusses the diagnostic differentiation of this infection from the condition of " milker's nodules ", which may affect both man and cattle. He considers that as cowpox is still fairly common in cows in the West of England it may be encountered more frequently as a human infection owing to the decline in vaccination in infancy. (A useful summary of the early history of vaccination is given in the introduction.)

J. E. M. Whitehead

854. **A Water-borne Epidemic of Weil's Disease.** (Über eine Trinkwasserepidemie von Weilscher Krankheit)

M. RANKOV. *Zeitschrift für Hygiene und Infektionskrankheiten* [*Z. Hyg. InfektKr.*] **140**, 556–572, 1955. 4 figs.

The author reports an epidemic outbreak of Weil's disease which occurred at Stari Bečej, Yugoslavia, in 1938. The disease is seldom found in that country, and the diagnosis offered some difficulties at the beginning as its clinical picture resembled those of both influenza and paratyphoid-C infection. Eventually, however, *Leptospira ictero-haemorrhagiae* was isolated from the blood. The epidemic was confined to one district and its source was traced to an infected well. In all, 390 persons were affected, 2% of whom died from the disease. Nearly 95% of those infected obtained their drinking water from the infected source. The remaining 5% did not use this well themselves, but had visited neighbours who did. The district was infested with rats.

The clinical picture of the disease was not typical in all cases, and in the majority jaundice and nephritis were absent. The highest incidence was in the age group 30 to 40 years; children up to the age of 5 were relatively unaffected, only 8 cases occurring in this age group. The author assumes, however, that this was due to their drinking less water and thus being less exposed to infection than the adults.

Franz Heimann

Industrial Medicine

855. **Crystallographic Methods in the Study of Silicotic Lungs.** (Apport des méthodes cristallographiques dans l'étude des poumons de silicose)
L. DÉROBERT, P. F. CECCALDI, A. RIMSKY, and A. OBERLIN. *Archives des maladies professionnelles, de médecine du travail et de sécurité sociale* [*Arch. Mal. prof.*] **16**, 101–107, 1955. 4 figs., 5 refs.

In an investigation carried out at the Institute of Industrial Hygiene of the University of Paris a large silicotic nodule from the lung of a victim of the disease was calcined below 600° C. and the ash subjected to *x*-ray powder analysis by the Debye–Scherrer method, which is described in detail. The diffraction photograph obtained was that of quartz. [The α–β transition at 574° C. is not mentioned.]

The ash was also shaken up with water and allowed to settle for several hours, after which a portion of the supernatant fluid containing the finer particles still in suspension was taken and used for examination with an electron microscope, both directly and by electron diffraction. In contrast to *x*-ray diffraction, where the arcs on the photograph are produced by radiation scattered from a large number of small crystals, electron diffraction permits the examination of individual crystals, thus enabling traces of substances which are not present in sufficient quantities to be detected on a Debye–Scherrer photograph to be identified. It was confirmed that the ash was composed mainly of quartz, but minute traces of asbestos and mica, in crystals of characteristically fibrous and laminar shape, were also found.

Two years before the onset of the symptoms of silicosis the subject had worked for a year at sand-blasting, using sand consisting of almost pure quartz. Death occurred a year after the commencement of treatment for silicosis. Necropsy confirmed the diagnosis and chemical analysis showed the presence of 55 mg. of silica per 100 g. of fresh lung. [It is unfortunate that the total silica content of the lungs is not given, because this figure would be of interest in comparison with the occupational exposure.]

C. N. Davies

856. **The Control of Pulmonary Tuberculosis in a Group of Industrial Establishments**
G. F. KEATINGE. *British Journal of Tuberculosis and Diseases of the Chest* [*Brit. J. Tuberc.*] **49**, 3–8, Jan., 1955. 5 refs.

The incidence of pulmonary tuberculosis among 3,421 employees of factories and quarries in Derbyshire, Nottinghamshire, and Leicestershire was investigated. New entrants were subjected to a medical examination, including *x*-ray examination of the chest. The majority of entrants were under 36 years of age and almost three-quarters of the women were in the age-group 15 to 25 years. Eight cases of active pulmonary tuberculosis were detected, giving a rate of 2·5 per 1,000 compared with 3·3 per 1,000 recorded in mass miniature radiography Surveys (Ministry of Health, 1954). Only one female was suffering from an active infection, and in only one instance was there any evidence that the disease had been acquired by home contact with a tuberculous patient. It was believed that in most cases the infection had been acquired from sources outside the home and factory. Non-tuberculous or quiescent lesions were present in 14 other employees, who were given work compatible with the maintenance of good health. In spite of this precautionary measure there was renewed activity of the disease process in one instance. Of the entrants who had active infection, 3 were eventually placed in work after the disease had become quiescent.

Established foundry workers were subjected to routine chest *x*-ray examination, but other employees were examined radiologically as the occasion demanded. An attempt was made, however, to supervise the health of all young workers. Over a period of 7 years radiological examination of the chest was carried out in nearly 70% of the established employees. By this means 3 cases of active pulmonary tuberculosis were discovered. It is noteworthy that during the same period a considerably higher incidence of the disease was recorded by the local authorities of the area.

A. Garland

857. **Occupational Cancer of the Urinary Bladder in Dyestuffs Operatives and of the Lung in Asbestos Textile Workers and Iron-ore Miners**
G. M. BONSER, J. S. FAULDS, and M. J. STEWART. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **25**, 126–134, Feb., 1955. 21 refs.

858. **The Pathology of Rehabilitation**
P. B. S. FOWLER. *Lancet* [*Lancet*] **1**, 467–471, March 5, 1955. 1 fig., 6 refs.

This report on the factors which impede rehabilitation and resettlement after physical or mental illness is based on the study of 1,945 persons constituting a representative sample of the total register of disabled persons, set up in 1944 under the Disabled Persons (Employment) Act, for the south-east of England. Approximately 90% were men, and 60% were under some form of medical care; 716 (36%) were unemployed and 15% of the remainder were in unsatisfactory employment—more often for socio-economic than for medical reasons. In the author's opinion, one-fifth of the group studied were not truly " disabled persons " as defined by the Act and should not have been on the register at all since their disability had no effect on their performance of their normal work.

Resettlement was unsatisfactory in roughly half of those surveyed. The primary causes were considered to be: (1) age (resettlement was more than twice as difficult in persons over 40, and these constituted nearly half the

group); (2) psychological factors (more often hidden than open and accounting for one-quarter of the cases); and (3) lack of suitable employment or direction. Persons with medical disabilities such as bronchitis (8%), pulmonary tuberculosis (5%), peptic ulcer (6·8%), and cardiovascular disease (5·9%) were much more difficult to place than were those with physical—orthopaedic or traumatic—handicaps.

The author concludes that provision for sheltered work in the south-east of England is inadequate. He points out also that by the inclusion in the employers' 3% quota of persons improperly registered the truly disabled are put at a further disadvantage. Further, lack of proper direction leads to a wastage of man-power which, at a time of " full employment ", is not sufficiently appreciated and is increasing. *R. J. Matthews*

859. **Use of Edathamil Calcium in Treatment of Chrome Ulcers of the Skin**

C. C. MALOOF. *Archives of Industrial Health* [*Arch. industr. Hlth*] **11**, 123–125, Feb., 1955. 3 figs., 4 refs.

A new method of treating chrome ulcers of the skin by the use of a chelating agent has been found successful in 54 cases. An ointment containing 10% " edathamil " calcium-disodium (the calcium disodium salt of ethylenediaminetetraacetic acid) in a base of hydrous wool fat is applied to the ulcer for 24 hours, covered by a bandage. At the end of this time, or after a further 24 hours, the chromium-contaminated base of the ulcer is found to be loose and can usually be lifted out with forceps. The inflammation resolves very quickly and pain is relieved. Simple dressings (gentian violet has been found helpful) complete the cure. *M. A. Dobbin Crawford*

860. **Treatment of Acute and Chronic Lead Poisoning with Disodium Calcium Versenate**

J. F. WADE and J. F. BURNUM. *Annals of Internal Medicine* [*Ann. intern. Med.*] **42**, 251–259, Feb., 1955. 2 figs., 15 refs.

The calcium ion in disodium calcium versenate (disodium calcium ethylenediaminetetraacetate; Ca EDTA) is readily replaced by lead, copper, nickel, or cobalt because of the greater stability constants of the heavy-metal chelates. Moreover, Ca EDTA cannot chelate the calcium ion in plasma and so does not cause tetany. For these reasons this complex has been tried in the treatment of lead poisoning and has shown considerable promise.

In this paper from the Veterans Administration Hospital, Birmingham, Alabama, 5 such cases are described, in each of which the diagnosis of lead poisoning was confirmed by urinary analysis, a urinary lead excretion level of 0·1 mg. per litre or higher in 24 hours being considered abnormal. The drug was given intravenously in a daily dose of 0·5 to 2 g. in 500 ml. of normal saline over a period of one to 2 hours, the average total dose given over a 10-day period being 15 g. This treatment resulted in a 15-fold increase in the excretion of lead in the urine in all cases, the largest amounts being excreted in the 12 hours following the injection. The symptoms of lead intoxication disappeared within 2 hours of the first injection in 2 cases, and within 4 days in 2 more cases; in the 5th case the symptoms had subsided before treatment began. Basophilic stippled erythrocytes—which had numbered 19 and 12 respectively per 1,000 in 2 cases—disappeared before the end of the period of therapy in all cases, the serum bilirubin level returned to normal in the 4 cases in which it was raised, and other abnormal signs also disappeared. No precise correlation between the daily urinary excretion of lead and coproporphyrin III was found, but the latter determination was carried out quantitatively in only one case.

No toxic effects resulting from the use of Ca EDTA were observed in these cases. One of the patients acquired a gonococcal infection 4 weeks after completing the treatment, when the level of urinary lead rose to 0·21 mg. per litre, showing that the drug does not completely remove all lead from the body. (The authors add in a footnote that 14 further patients with acute or chronic lead poisoning have since been treated successfully with disodium calcium versenate.) *W. K. S. Moore*

861. **Toxicity of Ditertiarybutylmethylphenol**

W. B. DEICHMANN, J. J. CLEMMER, R. RAKOCZY, and J. BIANCHINE. *Archives of Industrial Health* [*Arch. industr. Hlth*] **11**, 93–101, Feb., 1955. 5 refs.

This paper records a series of animal experiments undertaken to determine the toxicity of ditertiarybutylmethylphenol (DBMP), with a view to determining the safe limits for its use as an antioxidant and preserver of fats and oils in foodstuffs and of waxes used in the coating of food wrappers and containers.

Given by stomach tube in acutely toxic doses as a 20% solution in corn oil to rats, rabbits, guinea-pigs, and cats, DBMP produced the symptoms of parasympathetic stimulation—salivation, miosis, restlessness, hyperexcitability, unsteadiness, increased urination, diarrhoea, tremors, and a more or less pronounced degree of paralysis of the hindquarters. Fatal doses caused complete loss of appetite for days, followed by respiratory difficulty and coma. Prolonged feeding experiments on rats showed that a diet containing 0·8% of DBMP causes anorexia, and that a diet containing 1% retards growth. No changes were found in the blood cells or haemoglobin level, nor in the clotting time of the blood. Some increase in the excretion of glycuronates was noted, also a slight decrease in the ratio of inorganic to organic sulphates excreted in the urine. Rats fed on a diet containing 1% of DBMP gained less in body weight than controls, although at necropsy a slight increase in weight was found in the brain and liver in the treated rats. This was not found in animals fed 0·8% DBMP; in these no anatomical pathology was discovered post mortem. The intravenous injection into anaesthetized dogs of a lecithin emulsion containing 20 mg. of DBMP per ml. in doses of 25 mg. per kg. body weight caused a sharp fall in blood pressure. This reaction was lessened by a prophylactic injection of atropine.

The conclusion reached is that DBMP is a " relatively innocuous material ". *M. A. Dobbin Crawford*

Forensic Medicine and Toxicology

862. **The Dellwood Fire**
M. E. Cox, B. F. Heslop, J. J. Kempton, and R. A. Ratcliff. *British Medical Journal* [*Brit. med. J.*] **1**, 942–946, April 16, 1955. 5 figs., 4 refs.

The medical and pathological features are described of the fire at the Dellwood Maternity Home, Reading, in April, 1954, in which all but 2 of 15 babies a few days old died. A boiler flue which ran beneath the floor of the nursery was the cause of a smouldering night fire which, when discovered, had set one cot alight and filled the room, measuring 20 × 12 ft. (6·1 × 3·6 m.) with smoke. A brave night sister removed the infants, one of which, severely burned, was already dead. Of the remainder, 9 died within 48 hours after the onset, which was delayed for varying periods, of attacks of cough followed by obstructive dyspnoea and cyanosis. Three others, who survived a few hours longer, developed pyrexia before succumbing to the same condition. Oxygen, aspiration of mucus, humidification, and chemotherapy were the mainstays of treatment.

Necropsy revealed membranous bronchial casts, pulmonary congestion, interstitial emphysema, and later pneumonitis. All specimens of lung examined had developed anoxic sub-pleural petechiae or larger haemorrhages. Lipoid droplets were demonstrated in the foreign matter inhaled and gave the same staining reactions as distillates of painted wood and linoleum from the nursery. The findings were similar to those in other mass fire tragedies, and not significantly dissimilar from those following inhalation of certain war gases or of nitrous, sulphurous, or ammonia gases.

The authors' discussion of treatment emphasizes the uncertainty of prognosis in this type of case: although the victims may not appear to be seriously affected initially, the outlook is always grave and immediate treatment essential to any hope of recovery. But it is difficult to determine how far such therapeutic measures as administration of atropine or cortisone, humidification, and aspiration can be carried without increasing the risk and the mortality. *Keith Simpson*

863. **Medico-legal Studies of the Rhesus Antigens in Dried Blood-stains.** (Recherches médico-légales des antigènes sanguins du type Rhésus dans les taches de sang sec)
J. Ducos and J. Ruffie. *Acta medicinae legalis et socialis* [*Acta Med. leg. soc.* (*Liège*)] **7**, 111–119, July–Dec., 1954. 6 figs., 9 refs.

The authors present from the Medico-legal Institute, University of Toulouse, a study of the antigens in dried blood-stains. In this, blood of known groups was deposited on a non-absorbent surface, such as a pane of glass, and also on cloth, wood, and metal to determine the effect of different surfaces. The stains were then preserved under different conditions of temperature, light, and humidity. By means of determining the absorption of the appropriate antisera with the unknown stain, the authors claim that a specific clear-cut result can be achieved for the factors C, Ctw, c, D, and E. They point out, however, that this applies only to large fresh stains on a non-absorbent surface, and that the results have to be interpreted with reserve in the case of small, old stains which have penetrated the substratum of the material. *Gilbert Forbes*

864. **Plasma Specific Gravity Changes in Sudden Deaths. Observations with Specific Reference to Drowning**
H. C. Freimuth and H. E. Swann. *Archives of Pathology* [*Arch. Path.* (*Chicago*)] **59**, 214–218, Feb., 1955. 5 refs.

Doubt has recently been cast on the reliability of the differences in the chloride content of the blood in the right and left atria as diagnostic of death from drowning, and it has been suggested that an estimation of the plasma specific gravity in the two chambers is a more reliable guide. The authors, working at Baltimore, Maryland, set out to investigate this, and now report the results obtained in 80 cases of death by drowning and in 80 control cases in which death was due to other causes. The diagnosis of drowning was based on the difference between the specific gravity of the left atrial plasma and that of the right atrial plasma. A negative result was taken as confirming that drowning had occurred. The authors point out that correction of the observed specific gravity values must be made for the contribution to them of haemoglobin resulting from haemolysis. In all 80 cases of drowning the result, after correction, was negative, this presumably being due to haemodilution by water; in death from other causes it was found that the result might be either positive or negative. The authors venture to conclude from this investigation that the finding of a positive value rules out the possibility that death was due to drowning. *Gilbert Forbes*

865. **Subpleural, Subpericardial and Subendocardial Haemorrhages. A Study of their Incidence at Necropsy and of the Spontaneous Development, after Death, of Subpericardial Petechiae**
I. Gordon and R. A. Mansfield. *Journal of Forensic Medicine* [*J. forensic Med.*] **2**, 31–50, Jan.–March, 1955. 9 figs., 7 refs.

The incidence of subpleural, subpericardial, and subendocardial haemorrhages was recorded in 891 unselected consecutive necropsies where the death had been notified to the Durban Magistrate because it was known or suspected to be due to non-natural causes or because the cause could not be certified. There was found to be no significant difference in incidence between males and females, but it was observed that the incidence of subpleural haemorrhages appeared to decrease with age

between birth and the adolesceet period, rising again among adults. Differences in the incidence of subpericardial haemorrhages were of no statistical significance. The authors claim that they have found petechial haemorrhages on the visceral surfaces of organs removed from the body which were not present before removal. They also record the spontaneous appearance of petechial haemorrhages under the visceral pericardium of the heart left *in situ* after death.

The observation is made that petechial haemorrhages may be found on the heart and lungs after death in all types of case, and the fact that they can develop after death is regarded as affording strong evidence that they cannot be of significance in diagnosing the mechanism of death.

Gilbert Forbes

866. **Salicylate Poisoning**

F. H. HARVIE and R. B. SINGER. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **89**, 149–158, Feb., 1955. 2 figs., 27 refs.

Three cases of salicylate poisoning, 2 in infants and 1 in a child of 4, admitted to the paediatric service of the Hospital of the University of Pennsylvania are described, the pharmacology, clinical features, and treatment of the condition are discussed, and a method of studying acid–base disturbances which permits the separation of respiratory effects from metabolic and renal factors is presented. The general sequence of events after absorption of salicylates is hyperventilation, followed by a consequent fall in plasma CO_2 content and pressure, and a rise in *p*H. If the dose has been large a primary metabolic acidosis rapidly follows—which, superimposed on the initial respiratory alkalosis, may cause difficulty in diagnosis. Large doses of salicylate first stimulate and then depress the central nervous system, causing initial excitement, disorientation, and convulsions followed by stupor and respiratory failure; death, when it occurs, is usually due to depression of the respiratory centre. Detailed histories of the 3 cases are given.

A technique is described for obtaining adequate samples of blood by heel puncture. On these, determinations of haematocrit value, whole blood CO_2 content, *p*H, and haemoglobin level were made; in some samples the plasma chloride and sodium levels were also determined. From these findings CO_2 content and CO_2 pressure in the plasma and the buffer base concentration of whole blood were calculated from the nomogram of Singer and Hastings. Buffer base is defined as the cation equivalent of the sum of all buffer anions in the blood, this being the amount that is available for neutralization of excess invading acids. The determination of this figure has certain advantages over the usual determinations of plasma CO_2 concentration or CO_2-combining power as a guide to therapy.

As regards treatment the authors point out that clinically patients suffering from salicylate poisoning may appear deceptively well when first seen, but gastric lavage should never be omitted unless it is certain that the dose was small. It is emphasized that sodium bicarbonate should not be used in lavage fluids since it increases the absorption of salicylates. Fluids, parenterally if necessary, are needed to combat the dehydration due to vomiting and sweating, and carbohydrate should be added to reduce the ketosis of starvation. Anticonvulsant drugs are better avoided because of the risk of causing a dangerous degree of central depression, but oxygen may be of value in reducing the possibility of cerebral anoxia. Alkalotic tetany should be treated by the cautious use of carbon dioxide in concentrations not greater than 5%, and intravenous calcium gluconate may also be given. Routine treatment should include the administration of vitamin K in large doses, ascorbic acid, and plasma albumin or whole blood to combat shock. Blood chemical determinations should be frequent and as complete as possible, measurement of the *p*H being obligatory. If the later phase of metabolic acidosis develops it should be controlled by the use of alkalis, the dose being less than that calculated to restore the buffer base or CO_2 content to normal. The authors draw attention to the special danger to young children of methyl salicylate (oil of wintergreen) because of its appetizing odour and the ease with which a large dose can be ingested, and urge that its use is best avoided in homes where there are small children.

P. N. Magee

867. **Carbon Monoxide Poisoning. Medico-legal Problems**

K. SIMPSON. *Journal of Forensic Medicine* [*J. forensic Med.*] **2**, 5–13, Jan.–March, 1955. 2 figs., 5 refs.

Writing from Guy's Hospital, London, the author emphasizes the ease with which deaths from accidental carbon monoxide poisoning may be overlooked in spite of the exercise of reasonable vigilance. In a series of 100 cases of accidental poisoning no fewer than 46 were unrecognized until post-mortem examination. The chief factors accounting for this are: (*a*) the circumstances of death do not always indicate the likelihood of exposure to carbon monoxide—a number of cases are described in which a distant source (not on the premises) was responsible; (*b*) deficient sense of smell in the investigator accounts for many cases being unsuspected; (*c*) disease, old age, and drunkenness may all be too easily assumed to be the cause of death when in reality they are often only contributory factors.

Three medico-legal aspects are discussed: (1) the difficulty of detecting low concentrations of carbon monoxide in the blood, especially of the elderly, the drunk, and those who are ill; (2) the danger, by misinterpretation of symptoms, of raising suspicion of crime where none in fact exists; (3) the rate of post-mortem dissociation of carboxyhaemoglobin, which is much slower than has been assumed in the past. A diagram is given in which the degree of saturation of the blood with carbon monoxide is related to the age of the individual. In the 100 cases, 49 of the victims were over 70 years old, 11 were suffering from active disease, and 7 were drunk. The HbCO saturation figures ranged from 23 to 52%. Several interesting case records are given in which the signs and symptoms were misinterpreted, and death was assumed to have occurred from causes other than carbon monoxide poisoning.

Finally, the author makes the important point that great technical care is not necessary to obtain reliable blood specimens and that a delay even of several days causes very little significant fall in the HbCO saturation value.

R. Wien

868. **Lead-poisoning in Children. Correlation of Clinical and Pathological Findings**

H. B. MARSDEN and V. K. WILSON. *British Medical Journal* [*Brit. med. J.*] **1**, 324–326, Feb. 5, 1955. 1 fig., 19 refs.

In this paper from the Royal Manchester Children's Hospital the authors describe 2 cases of lead poisoning in children, including the necropsy findings and various biochemical observations. In both cases vague symptoms developed towards the end of the second year of life, but in neither was the diagnosis made at that time. One child lived to the age of 4 years, when the presence of anaemia, constipation, abdominal colic, and punctate basophilia suggested the possibility of lead poisoning, but in the other case the diagnosis was made only post mortem. There was a history of habitual chewing of painted articles in the first of these cases, but none in the second.

On admission to hospital the first child was unconscious, with muscular tremors and excessive salivation, but no lead line was found on the gums. Glycosuria and amino-aciduria were present, the chromatographic pattern showing an excess of cystine, taurine, and especially β-amino-*iso*-butyric acid. No porphyrins were found in the small quantity of urine available. *X*-ray examination of the long bones showed increased density of the metaphyses. Lumbar puncture yielded clear fluid under increased pressure. The child died shortly after admission in spite of surgical decompression and attempts to reduce the intracranial pressure with hypertonic fluids. At necropsy the salient gross feature was a dense white band several millimetres wide seen in the diaphyses at the bone–cartilage junction. Microscopically, the liver showed extensive fatty vacuolation of all but the periportal parenchymal cells, many of the hepatic cell nuclei being swollen and containing inclusions, especially in the portal region. The kidneys showed fatty vacuolation of the tubular cells, with many nuclear inclusions in the proximal part. In the bones there was inadequate erosion at the bone–cartilage junction and broad, close-packed trabeculae were present in an area corresponding with the white band observed on gross examination. The presence of lead was demonstrated in the femur histochemically and chemically.

The second child, aged 1 year and 10 months, also showed evidence of raised intracranial pressure, including advanced papilloedema. Glycosuria and anaemia were present, but no punctate basophilia. Again death occurred rapidly in spite of decompression, and the post-mortem findings were essentially similar to those in the first case.

The authors discuss the frequent occurrence of glycosuria and amino-aciduria in lead poisoning and point out that the finding in their cases of evidence of damage to the proximal convoluted tubules confirms the work of Fanconi, who maintained that dextrose and amino-acids were absorbed at this site. They emphasize the importance of considering the possibility of lead poisoning in all children with vague cerebral symptoms or raised intracranial pressure, and stress the value for post-mortem diagnosis of examination of the cut end of a rib and of frozen sections of liver and kidney for intranuclear inclusions.

P. N. Magee

869. **An Outbreak of Lead Poisoning in the Canklow District of Rotherham**

J. A. GILLET. *Lancet* [*Lancet*] **1**, 1118–1121, May 28, 1955.

This is a full [and instructive] report of an outbreak of lead poisoning which occurred in December, 1954, at Rotherham, Yorkshire, as a result of the widespread use of discarded motor-car battery casings as domestic fuel. This practice brought 293 adults into risk of lead intoxication, but none was poisoned and only one, a girl aged 15, gave evidence of lead absorption. Among the 232 children under the age of 15 at risk, however, there were 55 cases of lead poisoning or absorption; of these, 51 children were under the age of 7, the youngest being an infant aged 10 weeks living in a poorly kept house. Two children aged 2 and 5 respectively had died the previous month, but lead poisoning was not suspected until 2 further cases had been diagnosed at the Children's Hospital, Sheffield. The bodies of the first 2 children were then exhumed and the true cause of death was discovered to have been poisoning by lead, the original cause of death having been given as idiopathic epilepsy, and cholaemia and infective hepatitis respectively.

An interesting account is given of the action taken by the public health authorities, including domiciliary investigation of the incidents, measures for education of the public, and disposal and after-care of the patients. Particular attention was given to the possibility of mental retardation as a sequel of lead poisoning in young children, intelligence tests being given to the affected children at intervals of 6 months while paediatric supervision continued. It was thought that lead absorption took place by the ingestion of lead contained in the ash from fireplaces, for no lead was found in the air of a room or in the flue gases of a stove when the conditions existing while the battery casings were being burned were reconstructed experimentally. Lead was found in the cinders and in the flue dust, however, in which it amounted to 12·5%. It is possible, also, that some of the younger children may have handled or sucked the fresh battery casings. The author concludes with a detailed description of these car batteries and a plea for a safer method of disposal of this dangerous waste material.

M. A. Dobbin Crawford

870. **Pathologic Changes Associated with the Use of Sodium Ethylene Diamine Tetra-acetate in the Treatment of Hypercalcemia. Report of Two Cases with Autopsy Findings**

H. R. DUDLEY, A. C. RITCHIE, A. SCHILLING, and W. H. BAKER. *New England Journal of Medicine* [*New Engl. J. Med.*] **252**, 331–337, March 3, 1955. 4 figs., 43 refs.

Anaesthetics

871. **The Action of Laudexium in Man and Experimental Animals**
A. R. HUNTER. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] **27**, 73–79, Feb., 1955. 12 refs.

Laudexium was used to produce relaxation in 86 patients anaesthetized by nitrous oxide and oxygen with a non-volatile supplement. It provided satisfactory relaxation during the operation, but the paralysis could not always be reversed by neostigmine. It had a profound effect on respiration and sometimes lowered the blood pressure, though only for a short period. In a subsequent laboratory investigation neostigmine was not completely effective as an antagonist to laudexium in the cat and mouse.—[Author's summary.]

872. **Clinical and Laboratory Experience with Ethyl Vinyl Ether**
W. H. L. DORNETTE and O. S. ORTH. *Current Researches in Anesthesia and Analgesia* [*Curr. Res. Anesth.*] **34**, 26–34, Jan.–Feb., 1955. 9 refs.

At the University of Wisconsin Hospitals, Madison, Wisconsin, ethyl vinyl ether was used as the main anaesthetic agent in 120 cases and in a further 100 for induction only. The open technique was used in the majority of cases. Generalized convulsions occurred in 3 children aged 2 to 9 years; in 2 cases there was inadequate relaxation and in 2 respiratory arrest. There were no deaths attributable to the anaesthetic. The authors consider that pharmacologically ethyl vinyl ether is more closely related to divinyl ether than to diethyl ether, but it does not impair liver function.

A. M. Hutton

873. **The Management of Children Undergoing Tonsillectomy. Premedication with Methylpentynol**
F. R. GUSTERSON. *Lancet* [*Lancet*] **1**, 940–943, May 7, 1955. 30 refs.

Some points in the management of children undergoing tonsillectomy are outlined, attention being drawn particularly to the importance of nursing and of anaesthetic technique in making a child's visit to hospital for operation as pleasant an experience as possible, especially if the child is under 5 years of age. Preoperative sedation in relation to depression of reflexes and control of restlessness after operation is discussed. It is pointed out that premedication with any of the barbiturates—whatever the route of administration—followed by opiates post-operatively may cause dangerous depression of respiration and protective reflexes.

Of a small series of 100 patients in the Worthing Group of Hospitals, 51 were given a barbiturate and 49 methylpentynol elixir, the dose of the latter being 2 fluid dr. (7 ml.) for children aged 2 to 4 years to 4 fl. dr. for children aged 8 to 10 years. In all cases anaesthesia was then induced with a "sleep dose" of thiopentone. The children given methylpentynol were less restless than those given the barbiturate and yet were better able to control their own airway even after they had received "nepenthe". A questionary issued subsequently to parents revealed no difference between the two groups in the child's reaction to the stay in hospital. Later, hyoscine added to the elixir was substituted for atropine to reduce secretion; the drying effect was satisfactory and sedation was increased. The author states that a sound film of this technique has been prepared.

[Probably the main value of this paper lies in the details of the management of the child in the 12 hours before induction of anaesthesia; these are not exhaustive, and experience has shown that by meticulous attention to all minutiae the proportion of children who are upset by premedication with atropine alone can be reduced well below the 20% mentioned by the author.]

Donald V. Bateman

874. **Phenothiazine Derivatives in Anaesthesia. A Report on 200 Administrations**
G. HARRISON. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] **27**, 131–138, March, 1955. 2 refs.

The author, from the United Leeds Hospitals, reports 200 operations in which phenothiazine derivatives and pethidine, with a relaxant if necessary, were the main anaesthetic agents. The 195 patients concerned were studied in some detail, and it is concluded that this method of anaesthesia is to be preferred to others because of the good operating conditions, the pain-free postoperative period, and the reduction of bleeding and sweating. [However, no scientific evidence, such as comparable data from a parallel series, is given for this conclusion.]

Ronald Woolmer

875. **Ouabain in the Treatment of Shock**
J. A. G. HORTON and M. H. A. DAVISON. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] **27**, 139–144, March, 1955. 6 figs., 8 refs.

The authors, at the Royal Victoria Infirmary, Newcastle upon Tyne, have used ouabain in the treatment of shock accompanied by myocardial depression to supplement volume replacement or to restore blood pressure without volume replacement. A total of 80 intravenous injections of 0·25 mg. of ouabain were given to patients undergoing major thoracic or abdominal operations. Following the injection the blood pressure rose in 67, fell in 9, and was unchanged in 4 cases. In most of the 9 cases in which the blood pressure fell the reduction could be ascribed to further bleeding or concomitant administration of depressant drugs. The authors recommend the administration of ouabain in cases of shock in which the response to intravenous fluid replacement is unsatisfactory, and as a prophylactic when deterioration is expected.

Ronald Woolmer

Radiology

EXPERIMENTAL

876. **The Experimental Background for Retroperitoneal Lymph Node Irradiation by Radioactive Colloids**
F. HINMAN, G. M. MILLER, G. I. SMITH, J. JAMES, E. NG, and G. SHELINE. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **100**, 345–350, March, 1955. 6 figs., 12 refs.

Working at the University of California School of Medicine, San Francisco, the authors have carried out experiments designed to determine the possible value of radioactive colloids in the treatment of metastatic tumours in the retroperitoneal lymph nodes. The movement of particulate matter within the retroperitoneal space was first investigated by injecting colloidal mercuric sulphide suspended in a colloid medium into the presacral space of dogs, the animals being killed and examined after 14 to 19 days. It was found that the dye had spread throughout the retroperitoneal space, with lymph-node involvement in a few cases as far as the subclavian lymph nodes. In a further study the injection of plain colloidal mercuric sulphide into the presacral space of guinea-pigs showed a rapid uptake in the lymph nodes, and the retroperitoneal space was largely cleared of the dye by the seventh day.

A suspension of lampblack was then injected retroperitoneally into 3 patients with testicular tumour shortly before the performance of radical lymph-node dissection. At operation 2 days later particles were found in the iliac nodes, and in one patient operated upon after an interval of 10 days lymph-node involvement was found above the aortic bifurcation. In further experiments on a dog 13 millicuries of radioactive chromic phosphate in 49 ml. of saline solution was injected into the presacral area. Surface counting for radioactivity 30 days later showed a maximum count at the injection site. The average blood level and urine output were 0·03% of the total dose per day. One hind leg became painful 15 days after injection, and muscular atrophy developed at a later date. Post-mortem examination 63 days later showed no untoward radiation effects, but a high level of activity was detected in the iliac and preaortic nodes. A similar study was carried out with radioactive colloidal gold.

The size of the particles injected appeared to be of importance. If these were very small, diffusion occurred into the blood stream, and if too large, no uptake into the lymphatic nodes occurred. The authors conclude that the retroperitoneal injection of radioactive substances, as used in these experiments, is likely at present to be of only limited value in the treatment of carcinoma of the testis in man, because of the possibility of causing local damage to tissues. They suggest nevertheless that this line of experiment may be worth pursuing.

A. M. Jelliffe

RADIOTHERAPY

877. **Supervoltage (2,000 Kilovolt Roentgen Rays) Irradiation with a Resonant Transformer Generator**
M. FRIEDMAN, J. DRESNER, and G. J. HINE. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **73**, 410–424, March, 1955. 11 figs., 11 refs.

The major physical advantages of supervoltage (2-meV) *x* rays for therapy are the reduced skin absorption and increased relative depth dose, enabling lethal doses to be delivered to deep-seated neoplasms. Three types of apparatus are available for the production of 2-meV *x* rays or equivalent radiation: (1) the electrostatic generator, (2) the resonant-transformer generator, and (3) the telecurie unit using radioactive cobalt. Although comparatively heavy, high, and bulky, the resonant-transformer generator has the highest output of the three (108 r per minute at a target–skin distance of 1 metre).

The resonant-transformer apparatus installed at the Hospital for Joint Diseases, New York, has a motor generator set delivering current at 180 c.p.s. and 440 volts which is multiplied in a transformer and further multiplied on the resonant principle. The tube is permanently evacuated and is of the multisection type. At the lower end there is an extension chamber containing target, water cooling jacket, and focusing coil. The first warm-up takes 20 minutes, but subsequently only 30 seconds are necessary to raise the voltage from zero to 2,000 kV (peak). The apparatus occupies a 3-storey building in the basement of which is the treatment room which houses the tank containing the transformer and tube. Above this is a well, two storeys high, housing the elevator mechanism and motor generator set. The beam can be placed at any angle, direction, and height from the floor. The tube is stable and its life long (4,000 hours at 1 meV, and 2,575 hours at 2 meV without deterioration). Dose distribution along the central axis was measured with thimble chambers and by film techniques. At a target–skin distance of 100 cm. and H.V.L. of 7·2 mm. lead with a 10×10-cm. field the depth dose was 57·5% at 10 cm., the air dose being 108 r per minute. The size of field is controlled by a shutter of intermeshing ¾-in. (19·1-mm.) lead plates bevelled to give the minimum penumbra with an 8×8-cm. field. The fields are positioned on the patient by means of a light beam from a projection lamp within the tube head.

With a single-portal technique, the absence of skin reactions is a danger, for although very high doses can be administered, the complications of dense subcutaneous fibrosis may be very serious. With opposing fields the same difficulty applies, the uniform irradiation producing a solid column of fibrosis. In irradiating the trunk damage to the intestines, liver, and kidneys may ensue,

and in the chest damage to the lungs. Opposing-field technique is now used only for the treatment of radiosensitive tumours displacing normal organs out of the pathway. With the multiple-portal or rotation technique, however, the full benefits can be realized. With the former, entailing small field size and extremely accurate aiming of the beam, very high doses can be achieved in the tumour. However, the irradiation is not homogeneous, and this difficulty is aggravated in tumours near the skin. This method is thus less efficient than rotation technique, which gives the most homogeneous dose distribution in the tumour, with minimal dosage to surrounding normal tissues and minimal volume dose.

It is emphasized that " with supervoltage radiation, one cannot apply the philosophy of radiation therapy based on the experience accumulated with 250 kV " and that new concepts of treatment are therefore necessary.

I. G. Williams

878. **A 50 Curie Cobalt 60 Teletherapy Unit**
W. H. FRY, H. MILLER, and K. F. ORTON. *British Journal of Radiology* [*Brit. J. Radiol.*] **28**, 8–12, Jan., 1955. 6 figs., 11 refs.

879. **Comparative Survival Times of *X*-ray Treated versus P^{32} Treated Patients with Chronic Leukemias under the Program of Titrated, Regularly Spaced Total-body Irradiation**
E. E. OSGOOD, A. J. SEAMAN, and H. TIVEY. *Radiology* [*Radiology*] **64**, 373–381, March, 1955. 3 figs., 14 refs.

A study was made of the survival times of 163 patients with chronic leukemias by the method of titrated, regularly spaced total-body irradiation. Twenty-three received spray roentgen irradiation; 140 were given ^{32}P. The prognosis for survival was not significantly different whether the total-body irradiation was delivered externally by the spray technic or internally from radioactive phosphorus, provided all other conditions of treatment were identical. The prognosis for survival of patients with leukemia treated by titrated, regularly spaced total-body irradiation, either with the spray technic or ^{32}P, is significantly better than that for a collected series including all radiation treated cases reported in the literature in the interval 1925 to 1951.—[Authors' summary.]

880. **Changes in the Human Leukocyte Count during X-ray Therapy for Cancer and Their Dependence upon the Integral Dose**
H. I. KOHN. *Radiology* [*Radiology*] **64**, 382–391, March, 1955. 3 figs., 29 refs.

The change in count of each kind of leukocyte was followed in 48 selected patients undergoing a conventional course of *x*-ray therapy, planned for four to seven weeks. The tumor dose varied from about 3,000 to 6,000 r; the integral dose varied from about 1 to 50 megagram-r. A table for the estimation of the integral dose is presented. A new unit, the specific integral dose (megagram-r/kg.), is introduced.

No significant change related to radiation dose was found for the basophil, eosinophil, or monocyte counts, or for the neutrophil count in patients receiving less than 10 megagram-r. In patients receiving more than 10 megagram-r, the neutrophil count, though variable, on the average fell to about 70% of its initial level by the middle of the treatment period, thereafter remaining at about that level. The lymphocyte count tended to fall gradually throughout the course of treatment. Although several exceptions were noted, for irradiation of the trunk, neck, and pharynx, the magnitude and rate of fall of the lymphocyte count depended primarily upon the integral dose and integral dose rate rather than upon the tumor dose or the kind of tissue irradiated. At integral dose rates of 0·25 to 1 megagram-r/day, the smaller the daily dose, the smaller the total integral dose required to reduce the lymphocyte count to 25% of its initial level. The minimum dose for this effect was about 7 megagram-r.—[Author's summary.]

881. **The Effects of Irradiation of the Pelvis in Patients with Carcinoma of the Cervix Uteri on the Iliac and Sternal Marrow and on the Peripheral Blood**
L. W. HUTAFF and H. W. BELDING. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **73**, 251–258, Feb., 1955. 2 figs., 25 refs.

At the Bowman Gray School of Medicine, Winston-Salem, North Carolina, the effects of irradiation of the pelvis were studied in 12 patients receiving radiotherapy for carcinoma of the cervix by examination of marrow aspirated from the sternum and the iliac crest, as well as by serial blood counts. In the blood, absolute leucopenia, neutropenia, and lymphopenia were observed, but lymphocytosis was never seen. The marrow from the ilium showed marked depletion of all marrow elements, while that from the sternum exhibited increased cellularity. Early in the course of treatment there appeared to be a transient lymphocytosis in the irradiated marrow. Possible mechanisms for these changes are discussed.

E. Stanley Lee

882. **The Results of Radiation Therapy for Recurrent Cancer of the Cervix Uteri**
M. VAN HERIK and R. E. FRICKE. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **73**, 437–441, March, 1955. 2 refs.

The usual impression among clinicians is that further treatment by irradiation of carcinoma of the cervix uteri which is recurrent after surgery or radiotherapy can only be palliative, but little information is available in the literature concerning the results of such re-treatment. All cases of carcinoma of the cervix with definite recurrences treated by radiotherapy at the Mayo Clinic between the years 1940 and 1947 have therefore been reviewed, an interval of at least 6 months between the primary treatment and the diagnosis of recurrence being required for inclusion of any case in the analysis.

Out of approximately 1,200 patients with carcinoma of the cervix, only 11 were treated initially by surgery alone and 3 by surgery after irradiation. The remainder were treated with radium and *x* rays, radium only, or (in one case) with transvaginal and external *x* rays. No

patient was treated by external irradiation alone. Of these 1,200 patients, 110 developed recurrent disease, of whom 90·9% had squamous carcinoma, 7·3% adenocarcinoma, and 1·8% other types. In 80% the disease recurred in less than 2 years and only in 3·5% more than 5 years after initial treatment. In all cases the recurrence was treated with radium (with surgery in addition in 4 cases). The 5-year survival rate after this treatment was 16·4% (18 patients) and the 3-year survival rate 27·7% (25 patients). The 5-year survival rates in relation to the site of recurrence are given as follows.

Site of Recurrence	No. of Patients Treated	No. Surviving 5 Years
Cervix or corpus uteri ..	5	3 (60%)
Vagina	2	2 (100%)
Cervix and vagina	4	2 (50%)
Cervix, vagina, and parametrium	47	5 (10·6%)
Parametrium	26	2 (7·7%)
Other..	26	4 (15·4%)
Total ..	110	18 (16·4%)

There thus seems to be a better chance of control or eradication of the recurrence if it is located within the more accessible pelvic organs—the uterus or vagina—than if it occurs elsewhere. Detailed study of the records of those patients who did not survive at least 3 years revealed that many received worth-while palliation.

I. G. Williams

883. **The Results of Radiotherapy in Carcinoma of the Cervix at the First Gynaecological Clinic of the University of Munich.** (Die Ergebnisse der Strahlenbehandlung des Kollum-Karzinoms an der I. Universitäts-Frauenklinik München)

H. EYMER and J. RIES. *Strahlentherapie* [*Strahlentherapie*] **95**, 367–369, Nov., 1954 [received 1955].

The authors summarize the 5-year results in 531 cases of carcinoma of the cervix treated during the years 1947 and 1948, and give comparative figures year by year for the period 1940–8; the results are also analysed in relation to Stages 1 to 4. The absolute 5-year cure rate for 1947 was 46·3% (246 out of 531 cases) and for 1948, 50·2% (239 out of 476). For the whole period 1940–8 the mean figure was 44·5% (1,557 out of 3,498 cases). The better results achieved in the later years are attributed to fractionation of radium treatment, and to individualization of combined radium and *x*-ray treatment.

J. Walter

884. **The Results of Treatment of Carcinoma of the Cervix, 1945–7.** (Ergebnisse bei der Behandlung des Uterus-Karzinoms in den Jahren 1945–1947)

H. BURGER and J. LEHMANN. *Strahlentherapie* [*Strahlentherapie*] **95**, 370–375, Nov., 1954. 7 refs.

During the 3-year period 1945–7, 385 cases of carcinoma of the uterine cervix were treated at the Gynaecological Clinic of the University of Tübingen, with an absolute 5-year cure rate of 42·6%. Only 26 cases were treated surgically, treatment in most cases being by a "modified Stockholm radium technique" plus external *x*-ray therapy. The results were the best in the history of the clinic and are attributed to the individualization of treatment, together with the use of antibiotics. The primary mortality was 2·86%. There was, however, an increase compared with previous periods in the incidence of fistula formation and of radiation injuries to the bladder and bowel.

In 97 cases of carcinoma of the body of the uterus treatment was primarily surgical if possible, followed in most cases by *x*-irradiation. If surgery was contraindicated, 4 applications of radium were made, plus external *x*-ray therapy. The 5-year cure rate for cases treated primarily by surgery was 65·6% and for those primarily by radiation 25·9% (7 out of 27), while for those given combined treatment it was 54·6%. Primary mortality was 6·2%.

J. Walter

885. **Cytological Prognosis in Cancer of the Uterine Cervix Treated Radiologically**

R. M. GRAHAM and J. B. GRAHAM. *Cancer* [*Cancer (N.Y.)*] **8**, 59–70, Jan.–Feb., 1955. 11 figs., 17 refs.

886. **Hypophysicteny with Radioactive Chromic Phosphate in Treatment of Cancer**

S. F. ROTHENBERG, H. L. JAFFE, T. J. PUTNAM, and B. SIMKIN. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat. (Chicago)*] **73**, 193–199, Feb., 1955. 1 fig., 9 refs.

The authors report experiments carried out at the Cedars of Lebanon Hospital, Los Angeles, in which the destruction of the hypophysis by the injection of colloidal chromic phosphate containing radioactive phosphorus was attempted. This substance emits only beta radiation so that the destructive effect is strictly localized. In an experimental study 1 mc. of the material in 1 ml. of solution injected into the brain of dogs was found to produce an area of necrosis about 0·5 cm. in diameter, and the material did not enter the blood stream to any appreciable degree.

The method was then tried on 6 patients apparently in the terminal stages of malignant tumour, 3 with carcinoma of the breast, 2 with carcinoma of the thyroid, and one with prostatic carcinoma. The pituitary was approached in the usual manner, a frontal flap being turned down and the dura opened along the sphenoid ridge. When the pituitary fossa had been displayed and all bleeding controlled, 2 ml. of the radioactive solution containing 10 mc. of chromic phosphate and slightly coloured with 1% methylene blue was introduced through a 5-cm. 25-gauge needle attached to a tuberculin syringe, the injection being made slowly over a period of about 2 minutes. The glandular tissue was seen to grow diffusely blue. Usually 3 or 4 punctures were made at different sites to secure uniform distribution of the fluid. Cortisone was given postoperatively and 5 of the patients were discharged from hospital 2 to 3 weeks after operation, from which they made a good recovery. The sixth patient died of acute pulmonary oedema on the second day, but necropsy showed the operation site to

be in perfect condition. In all other cases pain was relieved or reduced, one female patient being active and free from pain 3 months after operation. The 6 cases, which are described in detail, are all too recent to allow of any discussion of long-term results. For the procedure described the authors suggest the term " isotope hypophysicteny ". *E. Stanley Lee*

887. **The Radiotherapy of Chronic Arthritis, Spondylitis, Humeroscapular Periarthritis, and Epicondylitis.** (Die Röntgentherapie der Arthrosen, Spondylosen, der Periarthritis humeroscapularis und der Epikondylitis)
P. HESS and K. H. BONMANN. *Strahlentherapie* [*Strahlentherapie*] **96**, 75–81, Jan., 1955. 18 refs.

At Bethesda Hospital, Duisburg, Germany, 664 cases of " arthritis deformans ", including some spinal cases, were treated by *x* rays, 2 doses of 100 to 200 r being given at 3 days' interval and repeated once or twice after 6 to 12 weeks. The results showed that 12·6% of the patients were symptom-free, 43·8% improved, and 43·5% derived no benefit. These results were inferior to most of those reported in the literature. A closer investigation was therefore made, including a follow-up examination 6 months or more later. This showed a significant tendency to relapse although, conversely, improvement in some cases was delayed. In 364 cases followed up there was early or late improvement in 86%, a figure in general agreement with other published results. However, when the after-history was taken into account, this figure fell to 60%, and 14% remained completely refractory. In the authors' view lack of adequate follow-up appears to be responsible for the misleading impression given in most published series.

In humero-scapular periarthritis (now generally attributed to osteochondrosis of the cervical spine) treatment by radiation in 110 cases failed in only 13·8%. In 56 cases of epicondylitis (at the tendon insertions at the elbow) radiation treatment was unsuccessful in only 10%. The authors conclude that *x*-irradiation is the best treatment for all cases of this type.

J. Walter

888. **A Contribution to the Radiotherapy of Arthritis of the Knee-joint.** (Beitrag zur Röntgentherapie der Kniegelenkarthrosen)
K. KRAUTZUN and H. P. ELINGSHAUSEN. *Strahlentherapie* [*Strahlentherapie*] **96**, 82–85, Jan., 1955. 9 refs.

The authors point out that it is significant that there has recently been a tendency in irradiation therapy of arthritic knee-joints to decrease the dose, without apparently impairing results. In most cases symptoms are certainly not related to the degree of radiological change in the joint and are probably mainly dependent on secondary vascular effects. It seems reasonable, therefore, the authors suggest, to use methods that have proved valuable in leg ulcers, Raynaud's disease, scleroderma, and similar conditions, in which treatment has been directed to the autonomic nervous system, particularly as in more recent theories of aetiology vertebral osteochondrosis and Selye's adaptation syndrome have been mentioned.

On this basis, since 1946 all cases of arthrosis of the knee-joint have been treated at Knappschafts Hospital, Bottrop, Germany, by deep *x*-ray therapy directed in the first instance to the knee-joint itself. If this failed, the thoraco-lumbar sympathetic chains were irradiated by a spinal field on each side, 15×10 cm. in size, directed medially at 60 degrees, 150 to 200 r being given to each field. In climacteric cases in women, the pituitary region was sometimes also included, 100 r being given to each of 2 lateral fields, 15×10 or 10×8 cm. in area. Local treatment alone failed in 15% of cases; but when these cases were treated by the above techniques, 40% were rendered symptom-free or much improved, 35% improved, and 25% remained unchanged.

J. Walter

889. **The Treatment and Course of Malignant Melanoma.** (Therapie und Verlauf maligner Melanome)
L. NOSKO and S. TAPPEINER. *Strahlentherapie* [*Strahlentherapie*] **95**, 389–398, Nov., 1954. 2 figs., 25 refs.

This paper reviews 80 cases of malignant melanoma, 75 of which were histologically confirmed, seen in the 20 years 1933 to 1952 at the University Skin Clinic, Vienna. Of the 57 patients traced for follow-up, 10 had died of other causes and 23 (40%) were alive, 18 of whom had survived for at least 5 years, the relative 5-year survival rate thus being 31·6%. More than half (54·4%) already had metastases when first seen, emphasizing the importance of early diagnosis; of 26 patients without metastases, 9 survived for 5 years, while of 25 with metastases, as many as 7 survived for this period. In the authors' experience the best treatment is primary radical surgery followed by intensive irradiation, preferably with radium. They have found that local recurrence after this treatment is rare, and they express the view that melanoma seems to be relatively radiosensitive. Involved regional nodes were treated by deep *x*-ray therapy. Preoperative irradiation is probably valuable, but the numbers in this series were too small to allow of any definite conclusion on this point. Removal of naevi exposed to trauma is advisable.

J. Walter

890. **Counteracting the Acute Radiation Syndrome with Corticotropin (ACTH)**
K. W. TABER. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **73**, 259–264, Feb., 1955. 1 fig., 27 refs.

Writing from the Memorial General Hospital, Elkins, West Virginia, the author claims that good results in the relief of radiation sickness can be obtained by the administration of 10 mg. of ACTH daily, this treatment being continued until symptoms are alleviated and the course repeated if necessary. The tabulated results in 416 of the author's cases show that 47·6% obtained prompt complete relief, 34·1% delayed complete relief, 16·4% delayed incomplete relief, and 2% [not 19·2% as stated] no definite benefit. The author concludes that the use of ACTH has made it possible " to administer radiation therapy more intensively and in much higher doses through a grid without unwarranted discomfort to the patient ". *E. Stanley Lee*

RADIODIAGNOSIS

891. **A Modification of Sialography (Preliminary Report)**
P. RUBIN and I. BLATT. *University of Michigan Medical Bulletin* [*Univ. Mich. med. Bull.*] **21**, 57–63, March, 1955. 2 figs., 2 refs.

Post-evacuation radiographs are an important feature of several techniques in which radio-opaque medium is used but they have not previously been taken during sialography. At the University of Michigan Medical School, Ann Arbor, a suitable technique has been devised and applied in over 100 instances.

After application of 10% cocaine hydrochloride to the duct orifice dilatation is accomplished with olive-tipped probes, and a polyethylene catheter No. 60 is inserted for a distance of 3 or 4 cm. Introduction of the catheter is facilitated by a fine rigid wire stylet. "Pantopaque" is injected slowly until the patient experiences pain. The end of the catheter is then plugged with a wooden stopper and radiographs are taken. The catheter is removed and the patient sucks lemon for 5 minutes, after which time further radiographs are taken. If the initial filling is satisfactory, with minimal alveolar filling, a normal salivary gland should be completely empty within 5 minutes.

This method is recommended for determining local or general diminution of secretory function in a diseased gland. The authors stress the importance of correct filling in the interpretation of the post-evacuation appearances, since extensive alveolar filling will leave a residue even in a healthy gland.

[The method could also be used when it is desired to examine both sides at the same time, particularly in parotid sialography, where a heavy residue in one gland masks detail in the other in lateral projections.]

D. E. Fletcher

892. **The Diagnostic Value of the Deep Cerebral Veins in Cerebral Angiography**
B. S. WOLF, C. M. NEWMAN, and B. SCHLESINGER. *Radiology* [*Radiology*] **64**, 161–177, Feb., 1955. 22 figs., 5 refs.

In this discussion of the diagnostic value of visualization of the deep cerebral veins the authors state that with the use of serial films in performing cerebral angiography these veins are regularly visualized 4 to 6 seconds after injection. At the Mount Sinai Hospital, New York, it is their practice to take seven films in 8 seconds and the deep veins are usually seen on two successive frames. The terminal vein indicates the interventricular boundary between the thalamus and the caudate nucleus. The septal and caudate veins run immediately beneath the ependyma and indicate the extent of the lateral ventricle. The anterior portion of the terminal vein forms a loop round the anterior tubercle of the thalamus. The internal cerebral vein runs in the roof of the third ventricle.

The authors have found that the antero-posterior projection is the most useful for identification of lateral displacement of the internal cerebral vein, which is normally situated just to one side of the midline. Superoinferior and antero-posterior displacements of the deep veins are seen in the lateral view. The vein of Galen and its junction with the straight sinus rarely show significant displacement. Two types of displacement are found affecting the internal cerebral vein; the first, which is accompanied by obvious local distortion, is usually associated with relatively little lateral displacement and is produced by lesions immediately adjacent to the vein; the second is a displacement *en bloc*, with relatively little local distortion, and is produced by peripheral expanding lesions. The most marked lateral displacements are produced by large masses affecting the anterior pole of the brain.

Smaller displacements which are not obvious visually may be measured by means of a constant ratio scale. But displacements determined by measurement alone must be evaluated carefully and neglected if they are the only findings., since small degrees of rotation of the skull can produce errors. The changes described may occur in conditions not often examined by angiography, such as cerebral atrophy, agenesis of the corpus callosum, cerebral oedema, and other congenital abnormalities. It is pointed out that the information obtained from the venous phases is in general supplementary to that from the arterial phase; however, some diagnostic features may be confined to the venous phase.

John H. L. Conway Hughes

893. **Indications for Thoracic Aortography**
W. FALHOLT, G. THOMSEN, and H. G. DAVIDSEN. *Thorax* [*Thorax*] **10**, 23–26, March, 1955. 3 figs., 16 refs.

Thoracic aortography is considered to be indicated in the following circumstances: (1) suspicion of a small patent duct with an atypical murmur, when a duct could not be demonstrated by cardiac catheterization; (2) cases where the differential diagnosis between patent ductus arteriosus and an aortic septal defect could not be established by cardiac catheterization; (3) coarctation of the aorta, where the clinical examination or radiograph was suspicious of a complicating cardiac anomaly; (4) congenital anomalies of the aorta, double arch, aortic ring, etc., where surgical treatment is intended; (5) diseases of the heart, where the clinical and radiological examinations do not explain the murmurs found, and where an aortic disease must be suspected.—[Authors' summary.]

894. **The Demonstration of Left Atrial Enlargement by Body Section Radiography**
B. H. PASTOR, G. T. WOHL, and L. T. LAWRENCE. *Circulation* [*Circulation* (*N.Y.*)] **11**, 400–403, March, 1955. 5 figs., 4 refs.

The authors, from the Veterans Administration Hospital, Philadelphia, make a plea for the greater use of body section radiography (tomography) in the study of the heart. In tomograms taken in the antero-posterior and right anterior oblique planes they were able to demonstrate an enlarged left auricle in cases in which

no abnormality was found by the routine methods of examination. In this way, they claim, the elevation and compression of the main-stem bronchi are shown to better advantage. They suggest that tomography is of value in all cardiac conditions where the heart shadow is obscured by intracardial calcification. *B. Green*

895. **Studies in Angiocardiography: the Problem of Injection. Presentation of a High-pressure Automatic Injecting Machine to Meet the Needs of Modern Angiocardiography**
A. RODRÍGUEZ-ALVAREZ and N. DORBECKER. *American Heart Journal* [*Amer. Heart J.*] **49**, 437–454, March, 1955. 7 figs., 41 refs.

896. **Dysphagia Associated with Sclerosis of the Aorta**
P. G. KEATES and O. MAGIDSON. *British Journal of Radiology* [*Brit. J. Radiol.*] **28**, 184–190, April, 1955. 20 figs., 3 refs.

Dysphagia associated with pressure on the oesophagus from an unfolded aorta is a rare condition, the authors having found reports of only 3 cases in the literature. They now describe, with full clinical details, 7 cases collected from the records of the General Infirmary at Leeds, all of which were in women, 5 of whom were over 70 years of age. The pathogenesis of the condition and the various anatomical types of unfolding of the aorta are discussed, the radiological appearance and the site of obstruction of the oesophagus depending on which type is present. In 6 of the 7 patients left ventricular hypertrophy was evident, and it is thought that this was a contributory cause of the dysphagia.

Oesophagoscopy was performed in 3 of the cases with a view to excluding any other causes of dysphagia. The authors point out that, although the appearances described are quite common in the elderly, only a small proportion will complain of dysphagia.

Sydney J. Hinds

897. **Vascular Appearances in Subdiaphragmatic Pneumotomography.** (Images vasculaires pneumostratigraphiques sous-diaphragmatiques)
G. GIRAUD, P. BÉTOULIÈRES, H. LATOUR, and M. PÉLISSIER. *Montpellier médical* [*Montpellier méd.*] **46**, 375–389, Dec., 1954. 11 figs., 1 ref.

In describing their method of performing subdiaphragmatic pneumotomography, as developed at the Faculty of Medicine, Montpellier, the authors stress the importance of injecting the air slowly and gently. With the patient in the genu-pectoral position a total of 800 to 1,500 ml. of air is injected into the precoccygeal region over 20 minutes. The exact centring of the tube is achieved under radiographic control and a narrow cone is used for taking the radiographs, tomograms being made in the vertical, and the median and paramedian sagittal planes.

Among the directly demonstrable vessels are the inferior vena cava and the aorta throughout their whole length. Round these are grouped the various viscera and minor vessels, the right and left renal arteries, the splenic artery, the arterial axis of the superior mesenteric artery, and the portal vein. A description of the pneumotomographic appearances of these structures, each with its own illustration, is then given. It is claimed that the tomograms may also show subdiaphragmatic adenopathies of various origin. *A. Orley*

898. **Bronchography in Pulmonary Tuberculosis Using Dionosil Oily**
W. S. HOLDEN. *British Journal of Radiology* [*Brit. J. Radiol.*] **28**, 100–103, Feb., 1955. 5 figs., 6 refs.

The author used "dionosil oily", the *n*-propyl ester of 3:5-diiodo-4-pyridone-N-acetic acid in pure arachis oil, as the medium for bronchography in 174 cases of pulmonary tuberculosis at the United Oxford Hospitals and Peppard Chest Hospital, Henley, a total of 240 bronchograms being obtained. This medium is readily absorbed and is less irritant than water-soluble media; moreover, there is no liberation of free iodine. Some of the details of the method of investigation are described. The cricothyroid route is used, and with the patient erect three routine films are taken in the postero-anterior, oblique, and lateral projections. After examination the patient is encouraged to cough and postural drainage is advised. No idiosyncrasy to the medium has been observed and complications are rare, the commonest being a tendency for the patient to cough a little more for a few days. In one case, which is described, bronchography was carried out 2 days after refill of a pneumoperitoneum. The patient developed a pneumomediastinum and had to be admitted to hospital where, however, she recovered within a few days. As a result of this experience the author advises against bronchography soon after a refill.

[While the author used 5 to 7 ml. of 10% cocaine for tracheal anaesthesia, it is generally considered that "xylocaine" (lignocaine) is less likely to give rise to toxic reactions. Don has recently described his experiences with dionosil aqueous in pulmonary tuberculosis (*J. Fac. Radiol.* (*Lond.*), 1955, **6**, 189).]

Sydney J. Hinds

899. **Tissue Reaction in the Lung after Bronchography with Water-soluble Contrast Media.** (Zur Frage der Lungengewebsreaktionen nach Bronchographie mit wasserlöslichen Kontrastmitteln)
D. WITTEKIND and J. HARTLEIB. *Frankfurter Zeitschrift für Pathologie* [*Frankfurt. Z. Path.*] **66**, 1–15, 1955. 6 figs., 23 refs.

After a lengthy discussion of previous reports in the literature concerning the damage caused to lung tissue first by oil-soluble and later by water-soluble contrast media commonly used in the performance of bronchography the authors describe a study carried out at the Institute of Pathology, University of Frankfurt, in which the lungs of 35 patients on whom bronchography had been performed were examined either after resection or post mortem. They found some confirmation of the reports that water-soluble contrast media produce a certain morphological reaction in the parenchyma of the lungs in the form of foreign-body granulomata.

They point out that the amount of contrast medium remaining in the alveoli depends largely on the general

condition of the patient, less being expelled in cases in which respiration is weak either because of the general weakness of the patient or because of neoplastic infiltration of the phrenic nerve; bronchial stenosis also tends to promote retention of the medium and to increase its viscosity. However, they have not encountered a single case in which the use of a water-soluble medium has led to a decisive reduction in the respiratory surface—as was frequently described in the days of oil-soluble media. In their experience the respiratory surface suffers only a short-lived limitation of function, which disappears after 24 to 36 hours. Of 19 cases of bronchial carcinoma in which one or both lungs were examined histologically after bronchography with a water-soluble contrast medium, foreign-body granulomata were found in 6; these seemed to be in causal connexion with remnants of the contrast material. Giant cells were seen 4 days after bronchography, and in one case the contrast substance appeared in the veins and lymph channels in the vicinity of the bronchi. For the demonstration of viscous material the authors recommend a 12-hour differentiation test in 70% alcohol after staining with thiomine tartrate, when the mucous membrane becomes pale but the carrier substance retains its red colour. Their general conclusion is that although water-soluble contrast media do produce some reactions in lung tissue, these can be considered clinically harmless. *E. Forrai*

900. **The Clinical Investigation of the Portal Circulation, with Special Reference to Portal Venography**
M. Atkinson, E. Barnett, S. Sherlock, and R. E. Steiner. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **24**, 77–91, Jan., 1955. 7 figs., bibliography.

The authors report the results of percutaneous transsplenic portal venography which was successfully carried out at the Postgraduate Medical School of London in 35 of 40 cases in which it was attempted. The procedure was employed only on patients in whom the plasma prothrombin value and blood platelet count were normal; it was performed in adults under local analgesia, but children were given a general anaesthetic. The apparatus consisted of a Schonander biplane serial angiographic table, the radiographic factors being 400 mA, exposure 0·06 second at 85 kV in the antero-posterior plane and 400 mA, 0·08 or 0·09 second at 90 kV in the lateral plane. A fine lumbar-puncture needle, 0·75 mm. outside diameter and 7 cm. long, was inserted in the eighth or ninth intercostal space in the mid-axillary line and directed downwards at 45 degrees to the transverse plane until the spleen was felt; it was then pushed 2 cm. further, and if blood returned from the needle it was assumed that the point of the needle was in the spleen. Thereafter 50 ml. of 50% diodone was injected by manual pressure over a period of 7 to 10 seconds. Ten films were exposed in each plane at the rate of one per second, starting 2 seconds after the beginning of the injection. No serious after-effects were noted and of 7 spleens examined after splenectomy or at necropsy, only one showed an intrasplenic haematoma 10 days after the injection.

The 35 cases examined included 21 of portal cirrhosis, 7 of biliary cirrhosis, 2 of obstruction of the splenic or portal vein, and 5 of splenomegaly of various types without portal hypertension. In one case in which portacaval anastomosis had been performed, the shunt was demonstrated. The results showed that in the normal portal venogram all the contrast medium passed through the liver and only the splenic vein and the portal vein with its extrahepatic branches were outlined. In cases of intrahepatic portal venous obstruction a proportion of the flow passed via the collateral vessels, that is, the left gastric, the gastro-oesophageal, and the para-oesophageal veins, and the para-umbilical, inferior mesenteric, and lumbar vessels running from the spleen to the diaphragm and parietes were also outlined in some cases. The lumbar veins were particularly prominent in cases of extrahepatic obstruction. Portal venous thrombosis was found in 4 out of the 21 cases of portal cirrhosis, and of the 7 cases of biliary cirrhosis, 3 showed intrahepatic obstruction and a fourth thrombosis of the splenic vein.

In conclusion the authors state that portal venography proved a more reliable method of demonstrating the presence of oesophageal varices than either examination with a barium swallow or oesophagoscopy, or even the two in combination. Demonstration of a collateral circulation is evidence of portal hypertension, although a raised portal venous pressure may be found in patients with a normal portal venogram. Slowing of the portal blood flow occurs whenever a collateral circulation is present, but slowing is not a feature of portal hypertension alone.

[This excellent article is well illustrated, contains a concise review of the literature from 1947, and should be read in full.] *B. Green*

901. **Cholangiography. A Critical Analysis**
H. G. Kantor, J. A. Evans, and F. Glenn. *Archives of Surgery* [*Arch. Surg.* (*Chicago*)] **70**, 237–252, Feb., 1955. 10 figs., 21 refs.

The value of cholangiography is critically examined by reference to a total of 405 cholangiograms obtained in 158 cases admitted to the New York Hospital between 1947 and 1952. In 55 cases the cholangiogram was abnormal, the most frequent cause being a stone in the common bile duct; in 12 cases this was demonstrated postoperatively, and it is pointed out that a stone in the retroduodenal portion may be difficult to detect surgically. Spasm of the sphincter of Oddi was found in 35 cases, stricture in 6, and tumour in 8. In addition to the pathological findings, some special points in the normal anatomy of the biliary tract are discussed. Altogether 48% of the operative and 34% of the postoperative cholangiograms were unsatisfactory, but the authors believe that this was largely the result of lack of interest in the procedure on the part of both surgeon and radiologist. They consider that filling is better with water-soluble contrast medium than with iodized oil. The technique they now use is described and they express the hope that it will achieve more satisfactory results.
Sydney J. Hinds

See also Pathology, Abstract 618.

History of Medicine

902. **Jean Nicolas Corvisart (1755–1821) and the Foundation of French Clinical Medicine.** (Jean Nicolas Corvisart (1755–1821) und die Begründung der französischen klinischen Medizin)
E. F. PODACH. *Medizinische* [*Medizinische*] No. 8, 293–295, Feb. 19, 1955. 1 fig., 7 refs.

Although intended for the legal profession, the young Corvisart attended by chance one day, along with some medical student friends, a lecture by Antoine Petit, the famous physician and anatomist. This impressed him very much and a breach with his father soon after led him to join the staff of the Hôtel-Dieu in exchange for board and lodging. His zeal quickly attracted attention and on completing his studies in 1781 he became pupil and assistant to Dessault, one of the most renowned surgeons in Europe at that time. Nevertheless Corvisart experienced difficulty in finding a regular post and after a quarrel with the influential Madame Necker he became a physician to the poor in the district of St Sulpice. This gave him the opportunity of attending daily the visits of de Rochefort at the Hôpital de la Charité nearby. His progress thereafter was rapid. In 1786 he became professor of pathology in the Faculté de Médecine, in 1787 professor of physiology, and in 1788 of pharmacy as well. He followed this success by becoming a physician at the Charité, and soon de Rochefort was only too willing to delegate his clinical and teaching duties to his brilliant young assistant.

After de Rochefort died Corvisart introduced reforms at the Charité which led to the foundation of French clinical medicine. He grouped his beds into wards of serious cases, convalescent cases, and of those suitable for clinical demonstration. Every physician had a fixed number of patients allotted to him and had to see the case through and keep a full record. Corvisart himself arrived at the hospital at six o'clock every morning; he began his routine by listening to detailed reports, then examined every patient in the wards, gave his own recommendations, and lectured to the students. He was a kindly teacher and encouraged discussion. A post-mortem examination was made of every patient who died, for Corvisart was a firm believer in comparing diseased and healthy organs. One of his oft-quoted remarks was "no one illness is like another even when the disease is of similar nature". He enjoined his pupils to recognize a disease by physiological, anatomical, and physical tests and he furthered medical progress by introducing percussion. Although this procedure was first made public in Austria in 1761 it had been ridiculed everywhere, and Corvisart himself used it for twenty years before he revealed its purpose. The French Revolution affected the Charité little. Corvisart was the most renowned doctor in Paris and as a teacher had gathered round him the most promising pupils. In 1795 he was elected Professor of the Collège de France and in the same year became a member of the Academy of Sciences. In 1803 he was appointed physician to Napoleon and two years later was created a baron.

Although he was regarded as the most outstanding physician of his time, Corvisart was critized for his apathy towards writing. This he rectified in 1806 and 1808 when he published two works which made his name in medical literature: *Essais sur les maladies et les lésions organiques du cœur et des gros vaisseaux*, and *Nouvelle méthode pour reconnaître les maladies internes de la poitrine par la percussion*. His book on the heart contains the foundation of cardiac pathology and demonstrates the value of percussion. His second work describes at length the method of examination of the chest by percussion which he had been using for twenty years. From now on the method was adopted in France and England and spread throughout Europe. But Corvisart only lived to see its beginning, for he died in 1821 shortly after Napoleon, the man who was reported to have said that he did not believe in medicine, but trusted Corvisart. *Ruth Hodgkinson*

903. **Theodor Billroth and His Influence on Gastric Surgery**
G. E. MOLONEY. *Oxford Medical School Gazette* [*Oxford med. Sch. Gaz.*] 7, 7–12, 1955. 1 fig.

Christian Theodor Albert Billroth (1829–1894), the son of a Lutheran pastor, came of Swedish parentage. He graduated at Berlin in 1852 and then spent a *Wanderjahr* visiting Vienna, Prague, Paris, London, and Edinburgh. He returned to Berlin to practise surgery, but private practice was so poor that he took the post of assistant to von Langenbeck. In 1860 he was invited to the small school of surgery in Zürich as professor; there his reputation grew and in 1867 he was unanimously elected to the chair of Surgery in Vienna. His triumphs were won in Vienna and his clinic became a surgical Mecca.

In 1872 he performed the first resection of the oesophagus and in 1873 the first complete excision of the larynx. He carried out intestinal resection in a number of cases, and in 1891 performed the first interileoabdominal amputation. In the year 1881—the most important year for Billroth—he successfully carried out resection of the pylorus for carcinoma, followed by gastro-duodenal anastomosis. Péan in 1879 and Rydygier in 1880 had performed this operation without success. Billroth's patient survived for only four months, dying from multiple metastases. After this Billroth had two failures and popular feeling was so intense that he was stoned in the streets of Vienna. By 1891, however, he had performed 41 resections with 16 operative deaths.

The operation known as Billroth II came into being in 1885 as the result of a planned gastro-enterostomy in a debilitated patient. At the end of this procedure the patient was in such good condition that the pylorus was also excised and the duodenal stump closed. The

Billroth I operation became unpopular because of the frequent leakage at the " danger angle ". Billroth has been credited with saying, " My heart draws towards Billroth I, but my experience towards Billroth II ". There is now no fear of leakage in either operation and comparison of the short- and long-term results shows that the first operation is the more satisfactory, thus supporting Billroth's view. The Billroth-I operation was subsequently developed by von Haberer, Schoemaker in Holland, the Mayo brothers, and Morley in Britain.

Billroth combined dexterity, boldness, and ingenuity. Although a heroic surgeon, he would not operate unless there was a reasonable chance of success. His fine presence and powerful physique, his candour and lack of affectation impressed his fellow workers, who included Czerny, Eiselberg, and Mikulicz. He hated war and its horrors. He loved music, which he had at one time thought to make his profession, and became the friend of Brahms, Hanslick, and Johann Strauss.

Billroth suffered from chronic bronchitis; he died alone during a nocturnal attack of asthma. His funeral was one of the most impressive ever witnessed in a European capital. He was the only surgeon to have his portrait printed on the stamps of his country.

J. G. Bonnin

904. **Moses Maimonides (1135–1204).** (Moïse Maïmonide (1135–1204))

J. PINES. *Scalpel* [*Scalpel* (*Brux.*)] **108**, 293–297, March 12, 1955.

Maimonides was born at Cordova in 1135, and received his early instruction in philosophy and natural history in the Hispano-Jewish schools of Spain at the hands of the great Arab masters Averroes and Ibn Trifail. At the age of 25 years he left Spain for political reasons, travelling by way of North Africa, Ceuta, and Jerusalem to Egypt, where he finally settled in Fostat, today one of the old quarters of Cairo. In his earlier years he gave his attention mainly to religion and philosophy and published important works relating to the codification of the Talmud. On the death of his father he was obliged to earn his own living and so came late to the profession of medicine which, however, he practised so successfully that he was soon appointed physician to the Sultan. His reputation grew from day to day and in his last years, when he himself was ill and bedridden, the Arab physicians attached to the court often sought his advice. He had earlier refused an offer from Richard Coeur-de-Lion of England to join him as his physician on the Crusades.

In his medical writings, composed during the last 15 years of his life, Maimonides earned for himself the title of the Jewish Aristotle by bringing about the fusion of mediaeval Jewish science with that of the Arabs. He was the intermediary between the Greek philosophical systems and the scholastics, was famous for his lucidity of expression and exposition, and inspired the work of such subsequent Jewish philosophers as Spinoza and Mendelssohn. He was an advocate of, and himself practised, observation of the patient at the bedside, and his regard for the healing power of nature was truly Hippocratic. He preferred treatment by diet to that by drugs, and was one of the first to treat the mind as well as the body. More than a dozen works on medicine have been attributed to him, but some have not survived. Amongst the best known are his *Aphorisms from Hippocrates*, *Aphorisms from Galen*, *A treatise on poisons and their antidotes*, prepared for the Grand Vizier of Egypt (which was frequently quoted by Mondeville and Chauliac in the 12th and 14th centuries), and a *Regimen sanitatis* prepared for the son of the Saladin, Sultan of Egypt, the first example of a book of advice on personal hygiene. The young prince was subject to digestive trouble and fits of depression, and Maimonides' advice was therefore directed especially towards the strengthening of morale. His lesser works were concerned with the treatment of haemorrhoids, asthma, and sexual disturbances.

The influence of Maimonides persisted for several centuries. In their Latin translation his works were studied at the Universities of Padua and Montpellier, and his *Aphorisms* ran through five editions. He died in 1204 at the age of nearly 70 years and was interred at Tiberias in Israel in an imposing tomb which has survived almost intact to the present time. On it is the inscription: " From Moses to Moses there is no equal to Moses ". The great Arab physician Ibn Abi Oseiba (1203–69), the most renowned historian of Arab medicine, testified that in both theory and practice Maimonides was the most remarkable physician of his time.

D. P. McDonald

905. **Problems in the Application of Statistical Analysis to Questions of Health: 1700–1880**

G. ROSEN. *Bulletin of the History of Medicine* [*Bull. Hist. Med.*] **29**, 27–45, Jan.–Feb., 1955. Bibliography.

The application of the numerical method to the analysis of social phenomena in the 17th century initiated a development of first-rate importance, destined to prove very fruitful for the study of health and disease. Because these early statisticians concerned themselves with the ascertainment of basic quantitative data of natural life in the belief that such knowledge could be used to increase the power and prestige of the State, the new field of endeavour was called political arithmetic. Its father was William Petty, who invented the term. His friend John Graunt made the first solid contribution (1662) when he brought to light a number of important facts—for example, that male births exceeded female ones, though there was eventual numerical equality of the sexes. He also attempted to construct a life table. The calculus of probability was developed by Bernoulli, who applied it to civil, moral, and economic conditions (1713).

France (1693) and Sweden (1748) first developed official population statistics, and the first census in the United States was taken in 1790. Germany and Britain lagged behind, though private efforts to collect and compare vital statistics were made in both countries. But the full effect of these public and private endeavours was not to be felt till the 19th century. Much of the information accumulated by the political arithmeticians was vague and imprecise, leading to ill-founded conclusions, though several efforts were made during the 18th century

to apply more precise mathematical methods to vital phenomena, notably by Laplace.

The early decades of the 19th century saw problems in the clinical and public-health fields being tackled increasingly by the statistical method. The physician Louis in France was concerned especially with clinical problems, and Farr and Guy in Britain with public-health problems. In 1848 Adolphe Quetelet, Belgian mathematician and astronomer, as a result of his contacts in France with mathematicians interested in the theory of probability and with physicians interested in the statistical study of health problems, developed his concept of the average man. He recognized that variation was a characteristic of all biological and social phenomena and that such variation occurred around the mean of a number of observations. He therefore developed a methodology which comprised the determination of statistical averages, the establishment of the limits of variation around an average, and investigation of the conditions under which variation would occur. Further improvements were made in the technique of statistical observation, but no other basic contributions to statistical theory and methods of analysis were made till Francis Galton and Karl Pearson opened up the most recent period in the statistical analysis of health problems.

H. P. Tait

906. **The Early History of Vital Statistics in Massachusetts**

J. B. BLAKE. *Bulletin of the History of Medicine* [*Bull. Hist. Med.*] **29**, 46–68, Jan.–Feb., 1955. Bibliography.

In 1639, nearly two centuries before the mother country, the General Court of Massachusetts established civil registration of marriages, births, and deaths, but the law was rarely enforced. In the early 18th century attempts were made in Boston to obtain figures for the incidence and mortality of smallpox and to evaluate vaccination. After the Revolution the American Academy of Arts and Sciences (1780) and the Boston Medical Society (1781), which was later to become the Massachusetts Medical Society, came into being, having among their objects the promotion and encouragement of medical discoveries. Wigglesworth in 1792 submitted to the Academy a life table for Massachusetts and New Hampshire based on bills of mortality. Despite its shortcomings, this was the first significant American contribution to vital statistics. In 1810 the Boston Board of Health required superintendents of burial grounds to report weekly the name, age, sex, and cause of death of each person interred, and after a year the Board published an abstract, and continued to do so for several years thereafter. The causes of death given were, however, often unsatisfactory. In 1837 the Boston Medical Association persuaded the City Council to adopt a satisfactory nomenclature and to require death certificates from physicians. The developments in Boston and the reports of work on vital statistics from Britain and France led Lemuel Shattuck to found the American Statistical Association in 1839. In 1835 Shattuck had published a chapter on statistics in his *History of the Town of Concord*, and he made an important contribution in his paper "On the Vital Statistics of Boston" (1841).

In 1842 the General Court of Massachusetts, instigated by the Massachusetts Medical Society and by Shattuck, required town clerks to prepare annual returns of births, marriages, and deaths. Although not altogether satisfactory, this Act first established the principle in the United States that vital statistics should be returned to the State Government for abstraction and publication. Spurred on by Shattuck, the Court further improved the law in 1844. In 1846 Shattuck published his census of Boston, a model of what a statistical report should be. Still he prodded the State legislators to improve their laws for the collection of statistics, and they did so again in 1849 and in several subsequent amendments, resulting in a steadily increasing completeness of information. Particularly striking was the improvement in Boston's statistics. In 1850 the *Report of the Sanitary Commission of Massachusetts*, Shattuck's great work, was published, in which he stated that the most important laws for ascertaining the facts regarding the sanitary condition of the State were those relating to the registration of births, marriages, and deaths. He recommended the creation of State and local health departments, extensive sanitary improvements, and many other public-health measures. Though the General Court failed to establish a State Board of Health until 1869, its first secretary looked back to Shattuck's report "as his inspiration and support".

Like other reformers, advocates of the registration of births, marriages, and deaths promised that acceptance of their programme would not only improve the public health but also reduce crime, poverty, and other social evils and increase the wealth, morality, and happiness of mankind. If, like other reformers, they were excessively sanguine, if their propaganda brought little change in public-health administration before the Civil War, they nevertheless were in the forefront of the public-health movement, and as such were, in the long run, among the most influential reformers in an age of reform.

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907. **The History of Teething in Infancy**

J. RENDLE-SHORT. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **48**, 132–138, Feb., 1955. 3 figs., 25 refs.

This is a review of medical opinion from the time of Hippocrates to the present day on whether the so-called teething troubles—diarrhoea, fever, convulsions, bleeding gums—can reasonably be ascribed to the process of cutting the teeth. In the past the standard of medical knowledge of the feeding and hygiene of infants was so low that the then supposed evil effects of teething can now all be attributed to infections, dietary deficiencies (particularly of ascorbic acid), and chronic mercury poisoning, calomel being in frequent use as a purgative for infants and also in the treatment of syphilis.

The author concludes by pointing out that, although abundant, adequate cause can be found for the local and general manifestations which were formerly generally ascribed to "teething", there still remains the question whether teething in itself ever causes symptoms.

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